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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

MARCH, 1931

ORIGINAL ARTICLES.

THE "THYROID HEART" WITH LOW BASAL METABOLIC RATE.

By Roger S. Morris, M.D.,

TAYLOR PROFESSOR OF MEDICINE, UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO.

In a recent paper, Levine[1] gives a valuable discussion of unrecognized hyperthyroidism masked as heart disease, and presents reports of a number of illustrative cases. In all of them, he found an increase of the basal metabolic rate of 33 to 74 per cent. None had exophthalmos or obvious goiter. The diagnosis was based on such data as the general appearance of the patient; warm, moist, hyperemic and slightly pigmented skin; greater comfort in cold weather than in warm; brief attacks of diarrhea or vomiting; great loss of weight; alert, quick movements; often a peculiar stare to the eyes and a tremor of the fingers; transient glycosuria.

Of the cardiac findings, he considers transient auricular fibrillation the most characteristic. The heart sounds are peculiarly hyperactive and loud. Failure to obtain the usual reduction in rate through digitalization is suggestive. "After a suspicion is aroused concerning the possibility of an unrecognized hyperthyroidism by one or more of the above criteria, a careful basal metabolism determination must be made. *If this is within normal limits, the diagnosis can be dismissed.*"* Coëxisting organic heart disease, such as angina pectoris, hypertensive heart disease or mitral stenosis makes the diagnosis even more difficult. The relief following subtotal thyroidectomy was either complete or marked improvement was obtained.

* Italics mine.

Hamburger and Lev[2] have also given an excellent discussion of the subject, with a review of the literature. They present their findings in 5 illustrative cases, all of whom had an increase in the basal metabolic rate, varying between +33 and +93. They discuss hyperthyroidism masked by congestive heart failure, by anginal heart failure, associated with organic heart disease of rheumatic or arteriosclerotic type, or masquerading as diabetes mellitus or as pernicious hyperemesis.

The foregoing picture, we believe, is not overdrawn, as we have had similar cases. We believe, however, that if undue emphasis is placed on the basal metabolic rate, which, like every other laboratory aid, is often misleading, many patients will suffer. We have repeatedly observed complete subjective relief or marked improvement following a subtotal thyroidectomy in patients whose metabolic rate was normal or subnormal.

Careful questioning in such cases usually discloses a preëxisting thyrotoxic state, in which the patients complained of nervousness, sweating, tremor, loss of weight, palpitation, weakness, *et cetera*. We have found this condition somewhat more frequently in patients with preëxisting toxic adenomata than in those with a preëxisting Graves' disease. The thyrotoxic state persists for a variable time and then it "burns out." It is during this later stage that the metabolic rate is apt to be normal or subnormal.

In many of the patients there is an obvious enlargement of the gland. If the enlargement of the thyroid is substernal, deviation of the trachea, an increase in the submanubrial dullness and, finally, Roentgen ray examination may lead to the correct diagnosis. In some instances, the goiter lies mainly behind the trachea, pushing it forward, as may be demonstrated by a lateral Roentgen ray film of the neck. Finally, it may be impossible, with our present means, to demonstrate a goiter before operation.

Hypertension has been common in our patients. There is a high pulse pressure with normal or slightly elevated diastolic pressure. The systolic pressure may exceed 200 mm. Often the pressure returns to normal, and in nearly all of our cases it has been markedly reduced, after the patient has had Lugol's solution and a subtotal thyroidectomy, excepting those in whom there is a widespread sclerosis of the arterioles.

The duration of the illness has been long in many patients, and the myocardium has often been permanently damaged. Yet it has been surprising to note the degree of improvement which has followed subtotal thyroidectomy, despite the low basal metabolic rate. Patients with extreme degrees of circulatory failure, with careful preoperative treatment, stand operation surprisingly well, as a rule. Needless to say, only a surgeon skilled in thyroid surgery should operate on such cases. A few illustrative cases are appended.

Case Reports. CASE I.—D. M. S., male, a physician, aged forty-one years, was seen first October 1, 1928. In 1917 he had extreme nervousness and palpitation for several months. He entered the army and was troubled with breathlessness, tachycardia and weakness. In 1919 he was given 5 Roentgen ray treatments over the thyroid. The tachycardia subsided and he felt well until the spring of 1927, when nervousness and tachycardia returned. There was also some tremor. He tired quickly. He had occasional sudden sharp pain in the precordium, radiating to the left shoulder, coming on during exertion. Basal metabolism in February, 1926 was −5; in July, 1928, it was −14. Thyroid extract ½ grain daily was prescribed, and after a five weeks' vacation, he felt well. But on resuming his practice, all of his symptoms returned. His usual and present weight is 205 pounds. In 1919 he weighed 175 pounds. The tonsils were removed in 1910. His previous health had been good.

Physical examination showed a large, well-developed man, weight 205, height 5 feet 10 inches. The color was good. There was no exophthalmos. There was a slight stare at times and a slight lagging of the upper lid on looking downward. There was no tremor of the fingers. There was no visible goiter. The neck was rather short. The thyroid, which was palpated with difficulty, seemed slightly enlarged and rather firm. The heart apex was not seen or felt. Relative dullness was 3 by 11.5 cm. Retrosternal dullness was 6 cm. The sounds were somewhat weak but clear and regular. The blood pressure was 132 systolic and 90 diastolic. The pulse rate, after being recumbent for ten minutes, was 90; after going up and down a flight of 25 steps it was 124; two minutes later it was 90. There was moderate dyspnea. The lungs were clear on percussion and auscultation. There was no enlargement of the liver and no edema of the ankles. An electrocardiogram was normal. Teleoroentgenogram showed slight enlargement of the left ventricle, no substernal goiter was seen and the trachea was in the midline.

Course. A month later, the patient entered the hospital. Examination of the teeth, sinuses and prostate were negative. The pulse rate varied between 90 and 100. The basal metabolism was now −4 and −6; the patient had been taking 1 grain of thyroid extract daily for several weeks.

On November 5, 1928, a subtotal thyroidectomy was done. The gland was much larger than examination prior to operation had indicated. It was a gland typical of hyperthyroidism, rather firm, with much scar tissue, probably the result of Roentgen ray treatment.

The patient made an uneventful recovery from operation and spent the winter in Florida. In the spring of 1929 he resumed his practice and has remained well. He has had no medication. Basal metabolism on November 5, 1930, was −10; teleoroentgenogram of heart normal; blood pressure 120 systolic and 80 diastolic; pulse, 76.

CASE II.—Miss X., aged fifty-four years, was first seen January 5, 1927, complaining of "fast beating of the heart."

Her tonsils had been removed four or five years ago. There was no history of rheumatic fever.

In May, 1927, the patient noticed swelling of her ankles; she consulted a physician who prescribed digitalis. The edema cleared up after about six weeks. She had also had dyspnea on exertion. At times she was aware of a rapid heart action, especially in her abdomen, when recumbent. She had lost strength and thinks she had lost some weight. She had felt nervous at times and occasionally a tremor had interfered with sewing. She had been unable to work since June.

Physical Examination. The patient was a well-developed woman of average size. There was no exophthalmos, lid lag or stare. There was no visible goiter. The right lobe of the thyroid was a little larger than a pigeon's egg and firm. The lungs were clear on percussion and auscultation. The heart apex was palpable in the fifth interspace 8.5 cm. to the left. Relative dullness was 3.5 by 10 cm.; retrosternal dullness 6 cm. The sounds were forcible, regular and clear. There was a faint systolic murmur audible at all valve areas. There was no accentuation of the second pulmonic sound. The pulse rate was 110; blood pressure 148 systolic and 88 diastolic. The record of the pulse rate, kept by the patient's sister during recent weeks had shown it to be about 90 or higher. Abdominal examination was negative except for strong pulsation in the abdominal aorta. The knee jerks were exaggerated. There was no edema of the ankles.

Course. The patient entered the hospital for observation. Determination of the basal metabolic rate gave readings of −11 and −12. Subtotal thyroidectomy was performed, and both lobes were found to be adenomatous. Recovery from the operation was uneventful. The patient returned to work in September, 1927. She was seen again in November, 1928 and had remained free of symptoms. Relative cardiac dullness was 2 by 9 cm. The sounds were strong and clear. There was no murmur. The rate was 84. The blood pressure was 135 systolic and 80 diastolic. The metabolic rate was not determined.

CASE III.—Mrs. Y., aged thirty years, on September 27, 1930, was seen by Dr. Leon Schiff, complaining of rapid heart and goiter. About two years ago, following the rather sudden death of her father, she became very nervous, and about a month later, she was told that her thyroid gland was enlarged. Basal metabolic rate on November 14, 1928, was −6; on January 28, 1929, it was −1 and −1.4. Since the onset, she had eaten more than formerly but had lost 10 pounds. She had palpitation at times. There was no history of rheumatic fever, chorea or sore throat.

On *physical examination*, the eyes were negative. In the isthmus and in the right lobe nodules about the size of an olive were palpated. There was a palpable systolic shock at the apex. Relative dullness was 3 by 10 cm.; retrosternal dullness 5 cm. The sounds were strong, clear, regular; rate 124. A soft systolic murmur was audible at the apex and pulmonic areas. The blood pressure was 136 systolic and 72 diastolic. The abdomen and lower extremities were negative. Basal metabolic rate was −16. Electrocardiogram showed *P–R* interval of 0.2 second; rate 110.

Course. October 14, subtotal thyroidectomy was done. There were multiple adenomata in the gland. Within one week following operation, the pulse rate had fallen to 70 to 80 and the murmur had disappeared. Blood pressure has been 120 to 126 systolic and 76 diastolic.

A considerable number of cases, similar to those cited, has been encountered. Many of them have had auricular fibrillation with marked congestive heart failure. *In the group under consideration the basal metabolic rate has been normal or subnormal; yet their response to subtotal thyroidectomy has differed in no way from that of patients with similar symptoms and an increased metabolic rate.* This seems to establish quite definitely that too much emphasis has been placed on the basal metabolic rate in the interpretation of clinical data. Many patients with "masked hyperthyroidism" will remain in this category if the metabolic rate alone is the deciding factor in diagnosis.

Conclusions. 1. The interpretation of clinical data should not be based on any one laboratory test.

2. Chronic heart disease is often of manifold etiology. When evidence of a preëxisting thyrotoxic state is found, even with a subnormal basal metabolic rate, subtotal thyroidectomy may be indicated.

3. Because of the great frequency of cardiac disease in patients with adenomata of the thyroid, particularly in patients of middle age or beyond, removal of adenomata before cardiac symptoms exist is indicated, as an important means of prevention of heart disease.

4. Auricular fibrillation is a common late manifestation of thyroid heart. If possible, patients should have operation performed before this develops.

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2. Hamburger, W. W. and Lev, M. W.: Masked Hyperthyroidism, J. Am. Med. Assn., 1930, **94**, 2050.

STUDIES OF RELATIVELY NORMAL OBESE INDIVIDUALS DURING AND AFTER DIETARY RESTRICTIONS.

By H. H. Fellows, M.D.,

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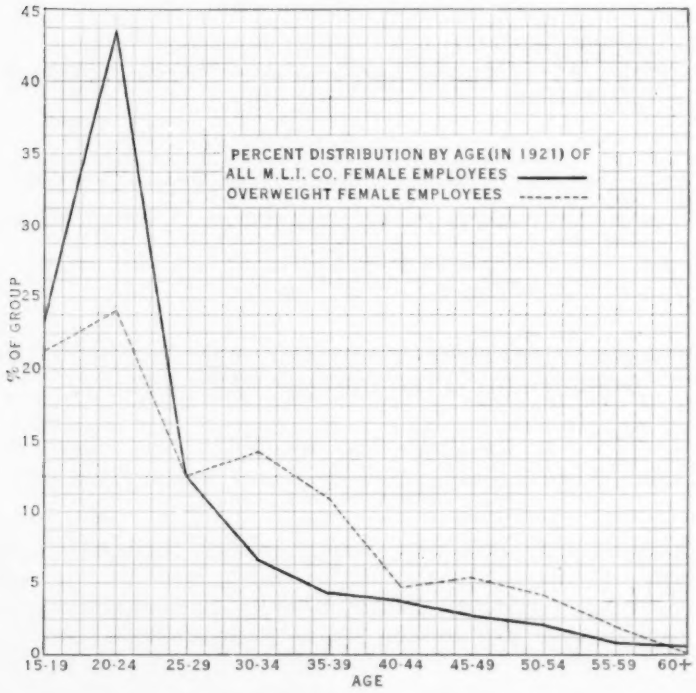
Among the 7530 Home Office employees of the Metropolitan Life Insurance Company in 1921, 558 or (7.4%) were 20% or more above average weight. Of these, 121 (1.6% of the total number on the payroll) were 40% or more above average weight. Approximately the same incidence of overweight was found among policyholders of the Metropolitan Life Insurance Company *under age forty-five* who were examined by the Life Extension Institute, but in those *over age forty-five* the incidence of overweight among the policyholders examined was much greater than among the employees. This difference may be due to selection within the group, since a large number of policyholders over forty-five who were overweight or otherwise impaired, asked for the Life Extension Institute examination.

Very largely because of the serious aspect of what should be a preventable and curable condition, the Metropolitan Life Insurance Company in 1922 decided to begin an investigation of overweight, and, starting in 1923, overweight employees at the Home Office were given an opportunity to attempt the reduction of weight under

the guidance of a physician. There were 294 employees who availed themselves of this opportunity.

Overweight among our employees tends to begin at about age thirty for the females, while among the males it tends to begin a little younger, but is not marked until age thirty-four (Chart I and II). However, in the group who voluntarily took treatment for their obesity, the onset of overweight was stated to have begun in childhood or at puberty in 58% of the cases.

CHART I.



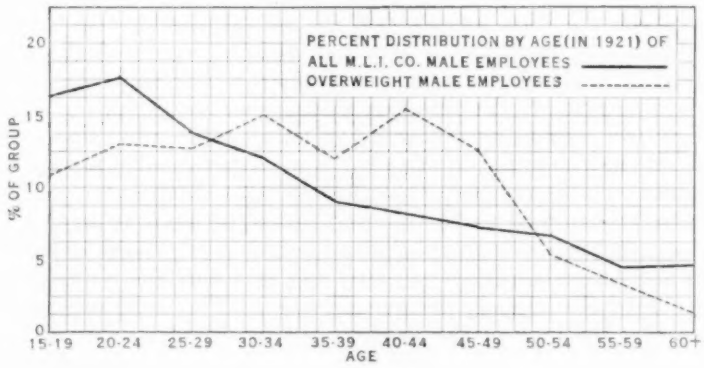
Before beginning weight control instruction, a thorough history was taken and a searching physical examination, including routine urinalysis and basal metabolism estimation, was made. During and at the close of the period of instruction a physical examination, basal metabolism estimation, and other laboratory tests were made.

All basal metabolism tests were carried out by the open-circuit method, a Tissot type gasometer being used to collect the expired air which in turn was analyzed in the Bailey modification of the Haldane-Henderson air analyzers. The tests were all made under rigidly controlled and standardized conditions in accordance with accepted technique. The open-circuit method was chosen for several reasons—it is simple and safe, the subject is comfortable

and at ease during the run, the apparatus can be checked and tested readily, and the data collected are complete enough for careful study.

Of the initial tests of the group, 211 (72%) were within the normal variation of ±10; 19 (6%) had rates above +10; 64 (22%) were below −10, and of these, 4 were below −20. When abnormal results were obtained, the test was repeated. During the course of observation, repeated tests were made on many cases. At the end of the weight reduction instruction, a comparison of the initial and final basal metabolic rates showed only a ±5 variation in 50% of the subjects, 34% showed a decrease of 6 or more, and 16% showed an increase of 6 or more. The cases showing a decrease in the final basal metabolic rate lost considerably more weight than the aver-

CHART II.



age. There was no consistent trend to the variation of the respiratory quotient in the various tests, nor can any generalized statement be made about its behavior.

Of the 294 individuals who undertook treatment for obesity, relatively few showed evidence of definite organic disease. Of the entire group, all but 33 could be classed as healthy adults. These 33 persons, however, did show abnormal findings; 13 had a moderate to severe degree of hypertension, apparently not associated with other disease; 17 had hypertension and definite cardiac involvement together with some arterial sclerosis; there was one case of a severe, though quite well compensated, double mitral disease; one case had had a dermoid cyst of the ovary removed and subsequent operation was necessary for removal of an infantile uterus and cystic ovary; there was one case of a moderate degree of hypertension together with severe migraine. The remaining 261 cases were classified as normal healthy adults at the time of examination.

The treatment of these individuals consisted almost entirely in the strict adherence to a reduction diet combined with carefully

directed exercises. A good deal of attention was paid to teaching each person the caloric content of all of the common foodstuffs and a fairly free choice was encouraged rather than advising the elimination of any one class of foods. It was thought that a restricted diet would suit the needs of each person better than a diet which eliminated special foodstuffs, and that a diet which had been so restricted could be more easily relaxed and with better results after weight reduction than could a diet in which certain foods were suddenly replaced.

To each patient was given detailed instructions together with a pamphlet containing a brief summary of the known facts regarding overweight, its mortality and morbidity, very complete food tables of all the common foods in 100-calory portions together with easy and practical, though accurate, measurements of these portions. Individuals were required to report weekly to the physician when careful consideration was given to the mental reaction and physical condition. At each visit a complete written report of all of the articles of food eaten during the week, together with the caloric value, was given to the physician in charge of the group.

Very few persons experienced any unfavorable subjective symptoms, though as would be expected, some complained of hunger and weakness. This uncomfortable feeling soon disappeared as they became accustomed to the reduced intake of food. Constipation was a rather common complaint and usually was present in persons who had been slightly constipated and in whom the reduced diet aggravated this already present condition. The usual methods of increasing the bulk of the stool by the use of agar or other inert substance together with small doses of mineral oil relieved nearly all such cases.

Thyroid extract was given in doses ranging from 1 to 3 grains a day to 18 individuals who were kept under very careful observation, checked by repeated basal metabolism tests. The results obtained by the use of thyroid were not brilliant and its use was discontinued in most cases long before the weight reduction had run any great length of time. There were a few persons having always a very low basal metabolism who felt better and lost weight more easily while taking small doses of thyroid, but the total number of such cases was small.

In handling this rather large group of persons, some observations were made which are interesting and yet cannot be explained fully. There has been considerable interest in the "glandular" type of obesity and it seems a certainty that there are individuals whose obesity if not actually due to, is associated with, endocrine imbalance. There were several individuals studied who seemed to belong to this group and the factors which characterized them were found chiefly in their clinical histories, though some evidence was found by physical examination. For instance, some of the women

stated that their obesity had become much more marked after puberty and felt that it was associated quite definitely with irregularities of menstruation. A typical history was that menstruation at the beginning was quite normal, but sometime later their periods became irregular and not infrequently would be absent for months or years, and at this time obesity became marked. One young woman had menstruated normally for seven years when menstruation ceased, a definitely masculine type of hair began to appear, she became obese, and six years later was operated upon and a large dermoid cyst of the ovary was removed. The majority of these individuals had a basal metabolism lower than normal. The group as a whole did not have any particular difficulty in controlling their weight, although some found it easier to reduce and felt better when taking small doses of thyroid extract. Theirs was a different experience than that of another group of patients who at all times showed an abnormally lowered basal metabolism and in spite of continued and honest efforts to reduce, maintained weight on an unbelievably low calory intake. One of these is a physician with a moderate degree of overweight who has always a basal metabolism varying between -33% and -36%, and even though exhibiting meticulous care and fortitude in carrying out a strenuous dietary program maintains weight on an intake of not more than 1200 calories per day.

While discussing the glandular type of individual it might be interesting to note that three of the women prior to presenting themselves for observation and treatment had taken large amounts of thyroid extract without consulting a physician. One girl had been taking 16 grains of thyroid extract a day for five years, another had taken one hundred 5-grain thyroid tablets and then discontinued because they made her nervous, and a third woman had been in the habit of taking 15 or 30 grains of thyroid extract whenever she felt like it. These were the only ones in the entire group who had used thyroid extract, although many had had experience with various advertised obesity cures.

The outstanding dietary abnormality was found in a young girl, aged twenty-four years, who when asked about her food habits said that she "ate nothing but sweets." When questioned further she stated that by that she meant that, actually, all she ate was either pastry, candy, cake, ice cream or sodas. Not quite believing this, and yet giving some credence to her statement, the physician placed her on a balanced diet containing 1200 calories. The first week she lost 8 pounds, the second week 7 more, and in the first eight weeks her weight reduction was 22 pounds. At the same time she said that she was eating more real food than she had ever had before and felt greatly improved.

At the initial examination each patient was asked about the build and health of her parents. Unfortunately it was impossible to

obtain data concerning the build of 28 fathers and 15 mothers. It will be noted (Table I) that the incidence of overweight is greater among the mothers than among the fathers. According to the patients' definite statements, 58% of the mothers and about 43% of the fathers were overweight. In about one-fourth of the group of overweight patients, both parents were stout. In the group of 553 parents whole build was known and who were studied only because they had a child who was under treatment for overweight, the incidence of overweight is about eleven times greater than that of the general population. This substantiates the statement that hereditary tendency to type is a definite factor in the production of many cases of overweight.

TABLE I.—BUILD OF PARENTS.

		Father's build.							
		Total.		Overweight.		Average or underweight.		Build not known.	
		No.	%	No.	%	No.	%	No.	%
Mother's build.	Total	294	100.0	125	42.5	141	48.0	28	9.5
	Overweight	171	58.1	70	23.8	88	29.9	13	4.4
	Average or underweight	108	36.8	49	16.7	52	17.7	7	2.4
	Build not known	15	5.1	6	2.0	1	0.4	8	2.7

TABLE II.—MORTALITY OR MORBIDITY OF PARENTS.

		Father's mortality or morbidity.											
		Total.		Alive and well.		Dead or ill with:							
						Diabetes.		Heart disease.		Other cardiorenal.		Others and unknown.	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Mother's mortality or morbidity.	Total	294	100.0	134	45.6	11	3.7	33	11.2	25	8.5	91	31.0
	Alive and well	143	48.6	93	31.6	5	1.7	15	5.1	8	2.7	22	7.5
	Dead or ill with:												
	Diabetes	21	7.1	5	1.7	3	1.0	3	1.0	1	0.3+	9	3.1
	Heart disease	24	8.2	7	2.4	1	0.3+	1	0.3+	5	1.7	10	3.4
	Other cardiorenal	33	11.2	13	4.4	1	0.3+	3	1.0	3	1.0	13	4.4
	Others and unknown	73	24.8	16	5.4	1	0.3+	11	3.7	8	2.7	37	12.6

Table II gives the morbidity and mortality findings for the parents. This information was obtained both at the time their children as patients began taking treatment for obesity and five years later when 193 of the patients were again interviewed. The incidence of diabetes is high; 32 parents are dead or ill with this disease and

one would expect other cases to develop as the group becomes older. This is a little over 10% of those who had died or were ill; a very high percentage. In the Medico-Actuarial Study on insured lives published in 1912, diabetes accounted for only 5.3% of the deaths of persons over forty-five years of age *and* 50 pounds or more overweight. The incidence of illness or death from heart disease and from other cardiorenal diseases was a little higher among the parents of the overweight patients than in the insured group mentioned above.

There seemed to be no relation between the age at onset of obesity in the children and the build of the parents, nor between the general diet of the children and the build of the parents. This is contrary to what might be expected from their heredity and environment, for it has been thought that the overweight caused by hereditary transmission of type may be expected to present itself at an early age, and that early food habits predispose many children to obesity.

In the treated group the amount of overweight varied greatly. Some who were only slightly overweight wished to learn how to keep their weight down to normal, while others who were extremely overweight wished to reduce their weight. Consequently, the weights ranged from 3% to 89% over average. As might have been expected, those who continued longest with the treatment lost the greatest amount of weight.

The following table shows the amount of weight lost during treatment in the group of 294 patients:

Loss of weight.	No. of cases.	% of cases.
Total number of cases	294	100
None	57	19
1 to 9 pounds	83	28
10 to 19 pounds	78	27
20 to 29 pounds	43	14
30 to 39 pounds	19	7
40 pounds or more	14	5

Of the original group of 294, it was possible to examine 224 cases one year after completion of treatment. During treatment they had lost an average of 14.7 pounds per person. One year later it was found that 32% of them continued to lose weight. This group had lost an average of 10.2 pounds during treatment and in the following year they lost an average of 3.8 pounds. Those who gained during the year had lost an average of 16.9 pounds during treatment. The gain averaged 9.7 pounds, or 57% of the weight lost. In general those who had lost the greatest amount during treatment or who showed the greatest amount of overweight at the beginning of treatment regained the least.

There were 193 cases examined five years after completion of treatment; 21% continued to lose weight, 33% had regained 1 to 14 pounds, and 46% had regained 15 pounds or more since comple-

tion of treatment. The regain was most marked among those who showed the smaller amounts of overweight at the beginning of treatment. The group which continued to lose weight had lost an average of 10.2 pounds during treatment and five years after completion of treatment had lost an average of 8.9 pounds more. The group which showed a gain in weight five years after treatment had lost an average of 16.1 pounds during treatment and regained an average of 18.3 pounds in five years, a regain of 114% of the weight lost. For the whole group, 85% of the weight lost during treatment was regained at the end of five years. Several of those interviewed at this time stated that periodically they successfully undertook measures to control their weight, but that it required almost constant care to maintain any satisfactory result. It seems that weight can be reduced by following a strict régime, but that evidently it is difficult for people to discipline themselves sufficiently when they do not report to a physician regularly for observance of their progress.

Chart III.

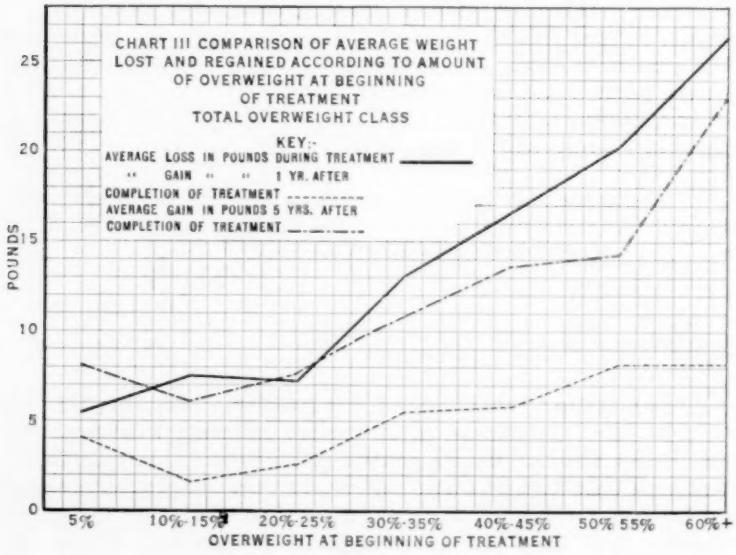


Chart III shows the average weight lost by the whole group according to the deviation from average weight at the beginning of treatment and the relative average amount of weight regained one year and five years after completion of treatment. Chart IV shows the similar findings for the group which lost from 1 to 15 pounds, and Chart V for the group which lost from 16 to 66 pounds.

It has been interesting and instructive to follow this group of

CHART IV.

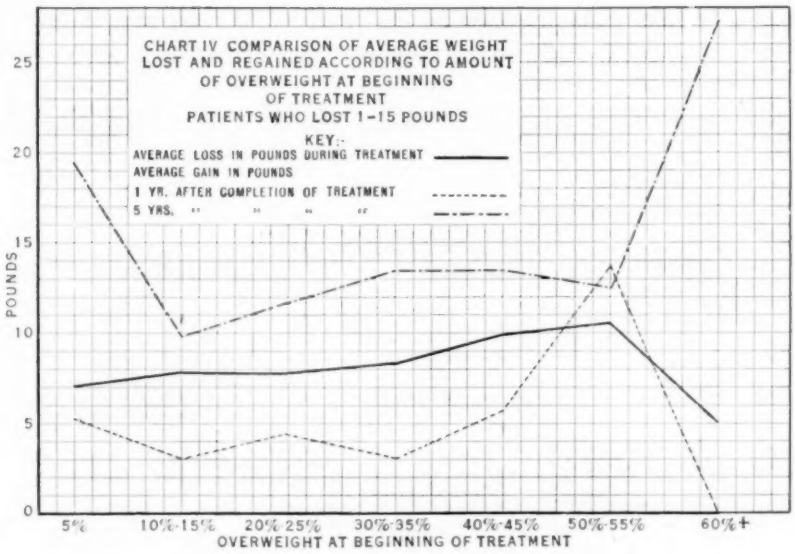
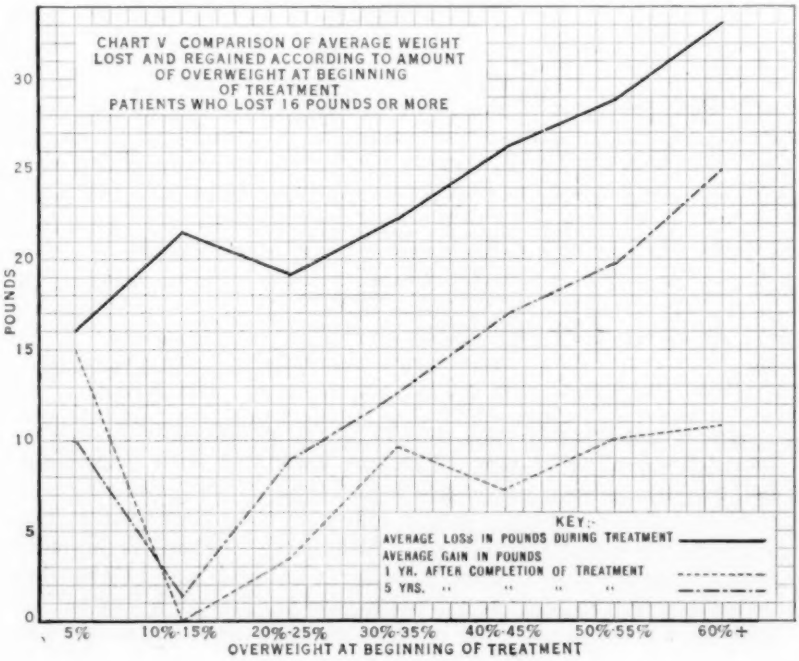


CHART V.



individuals for a period up to and including five years after they had made an attempt, some successful and some unsuccessful, to reduce their weight. The histories on the group of 33 cases who showed definite lesions when they began a reduction diet are given in Table III.

TABLE III.—THIRTY-THREE CASES ABNORMAL AT BEGINNING OF TREATMENT.

Sex.	% over average weight.				Findings on initial examination.	Subsequent history (five years after completion of treatment).
	Beginning of treatment.	End of treatment.	One year after.	Five years after.		
	%	%	%	%		
M.	34	32	31	..	Hy.	One year later died of angina pectoris.
F.	54	36	..	..	Hy. Cardiac involvement	Three years later developed diabetes and died in diabetic coma following severe sinusitis.
F.	17	2	2	6	Hy.	Glaucoma.
F.	5	-2	-2	..	Hy.	Attacks of angina.
F.	10	-2	-2	-3	Hy.	Hypertension increased, renal involvement.
F.	16	12	16	8	Hy.	Diabetes.
F.	2	-9	1	-4	Hy. Cardiac involvement	Worse.
M.	27	15	..	11	Hy. Glycosuria and cardiac involvement	Worse.
F.	48	29	29	40	Hy. Cardiac involvement and arterial sclerosis	Worse.
F.	51	24	40	44	Hy. Cardiac involvement and arterial sclerosis	Worse.
F.	57	37	37	50	Hy. Cardiac involvement	Worse.
F.	25	22	25	25	Hy.	Worse.
F.	41	23	27	32	Hy.	Worse.
F.	27	..	..	21	Hy.	Worse.
F.	42	..	39	39	Hy.	Worse.
F.	7	-1	-1	8	Hy.	Worse.
F.	51	34	38	41	Cardiac	Same.
F.	33	18	23	28	Hy.	Better.
F.	47	8	15	27	Hy.	Better.
F.	46	27	28	37	Hy.	Better.
F.	29	23	14	10	Hy.	Better.
F.	23	16	19	21	Hy.	Better.
M.	12	4	5	6	Hy.	Better.
F.	47	20	28	26	Hy.	Better.
F.	59	58	62	83	Hy. Cardiac involvement	Better.
F.	54	46	52	44	Hy. Cardiac Involvement	Better.
M.	65	28	38	43	Hy. Cardiac involvement	Better.
M.	59	38	49	51	Hy. Cardiac involvement	Better.
F.	40	22	28	35	Hy. Cardiac involvement	Better.
M.	44	31	36	32	Hy. Cardiac involvement	Better.
F.	24	17	23	27	Hy. Cardiac involvement	Better.
F.	19	7	..	14	Cardiac involvement	Better.
F.	41	25	15	10	Glandular dysfunction	Better.

Hy. = hypertension.

It is encouraging to note that 17 (52%) of the individuals who had definite physical signs of disease associated with overweight had suffered no progression and were better, symptomatically and clinically, five years after weight reduction than they were at the time of their initial examination. All but two of these have maintained a considerably lowered weight. It has been noted by several physicians that in treating the obese who also have a hypertension that there is uniformly a fall in blood pressure attending a decrease

in weight. Not only was this true during the treatment of these employees, but this lowered tension and generally improved condition has persisted five years after weight reduction.

Of the original group of 261 who at initial examination showed no signs of organic disease, 160 have been followed at the end of five years. Two have died and 8 have developed abnormal findings (Table IV). The remaining 150 are classified still as normal, healthy adults.

TABLE IV.—TEN CASES NORMAL (EXCEPT FOR OVERWEIGHT) AT BEGINNING OF TREATMENT.

Sex.	% over average weight.				Subsequent history.
	Beginning of treatment.	End of treatment.	One year after completion.	Five years after completion.	
	%	%	%	%	
F.	57	40	41	..	Two years after treatment died following operation for gall stones.
F.	21	Did not take treatment		..	Had maintained overweight up to one year prior to diagnosis of tuberculosis. Died of tuberculosis three years after initial examination for obesity.
F.	42	14	..	..	Developed severe diabetes.
F.	14	−9	−13	−14	Developed severe mental depression associated with menopause.
M.	30	22	..	23	Transient glycosuria.
F.	33	15	23	12	Transient glycosuria.
M.	22	17	17	21	Transient glycosuria.
F.	54	24	38	..	Mental case. Increase in blood pressure.
M.	27	16	29	32	Increase in blood pressure.
F.	73	38	46	57	Increase in blood pressure.

Summary and Conclusions. 1. The parents of the overweight subjects of this study show an incidence of overweight ten times greater than that of the general adult population. Both parents were overweight in 24% of the cases. This tends to substantiate the statement that heredity plays a definite part in the production of some types of overweight.

2. The incidence of diabetes among the parents of this group of employees is twice that of the insured population over forty-five years of age.

3. Overweight in the individuals studied was present in both males and females before age thirty years.

4. About 75% of the group of 294 who undertook treatment established a definite weight loss while under observation. One year after completion of treatment, 224 of the group were examined; 32% had continued to lose weight and 68% had regained some of the weight lost. Five years after completion of treatment, 193 of the group were examined; 21% had continued to lose weight and 79% had regained in whole or in part the weight lost during the period of treatment. It is a relatively easy matter to reduce overweight, but much more difficult to maintain weight at a reduced level.

5. More than half of the 33 individuals who showed physical signs of disease before commencing weight control showed less evidence of physical abnormality five years after completion than at the beginning. Overweight patients suffering from hypertension with or without cardiac complication may be benefited for years simply by reduction of their overweight, and especially where weight at a lower level is maintained.

6. There was no consistent trend evidenced either in repeated basal metabolic rates or respiratory quotients, before, during or after weight reduction.

ACKNOWLEDGEMENT. It is a pleasure to thank Mrs. Margaret G. Stephens of the Home Office Medical Department for the most exhaustive study and competent assembling of the statistical material used in this article.

AN OUTBREAK OF TRICHINOSIS IN PENNSYLVANIA.*

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TRICHINOSIS or Trichiniasis is a rather rare acute illness, found all over the world, caused by the parasite, Trichina spiralis. The encysted larvæ were first observed by Teidemann in 1822; the parasite itself was discovered by Sir James Paget in 1835, and was given the name Trichina spiralis by Richard Owen. Bowditch, of Boston, described the parasite in man in America in 1842 and Joseph Leidy found it in American pork in 1847. It was not known to have pathologic significance until Zenker, of Dresden, described his classical case in 1860, and his studies, together with those of Leukhart and Virchow, established the main facts of the disease.[1]

The parasite exists encysted in the muscles of the rat, pig, wild boar, dog, fox, bear and badger. Experimentally, rabbits and guinea-pigs[3] are readily infected and, interestingly, also show an eosinophilia.[2] Cattle, sheep and horses are difficult to infect, and, as in birds, the parasites develop in the intestine, but rarely invade the muscles.[3] Five per cent to 50% of rats are trichinous.[3]

When the meat containing the encysted parasites is eaten, the capsule is digested in the stomach. The parasites, both by their own movement and propelled by the stomach, promptly move on into the small intestine where they mature in two or three days. By the third day the females are fertilized. They then burrow with one end of their body into the intestinal mucosa just far enough

* Read at a meeting of the Main Line Branch of the Montgomery County Medical Society.

so that the embryo when discharged will get into the lymph stream. The male dies and probably disintegrates. The male is 1.4 to 1.6 mm. by 0.004 mm., and the female 2 to 3.5 mm. by 0.006 mm., while the larvæ are 0.09 by 0.006 mm. (Figs. 1 and 2.)

Each female is thought to discharge 1000 to 1500 embryos into the lymph spaces. The embryos then pass through the lymph vessels and thoracic duct to the subclavian vein and are carried by the blood stream all over the body. They develop only in the muscles where they may be found as early as the ninth day. They set up an acute inflammatory process in the muscles where they are found with their long axis parallel to the muscle fiber—the young ones straight and the older ones coiled and encysted.

The parasite takes a basophilic stain and at first is surrounded by an infiltrate consisting of lymphocytes, neutrophilic and eosinophilic leukocytes, plasma and giant cells. The adjacent muscle fibers undergo cloudy swelling and fatty degeneration and lose their transverse striation. In fifteen days the embryo becomes 1 mm. long and coils up and encysts, the encystment being complete at the end of a month, though the cell wall is not completely formed until the eighth to the twelfth week. Some of the embryos are destroyed by phagocytes, as one sees disintegrated material surrounded by infiltrates scattered through sections.

TABLE I.—CASES OF TRICHINOSIS RECORDED IN UNITED STATES, 1842–1914.

State.	Cases.	Deaths.	State.	Cases.	Deaths.
California	91	9	New York	355	62
Connecticut	14	5	North Carolina	1	
District of Columbia	1	1	Ohio	70	12
Illinois	90	24	Oregon	19	1
Indiana	64	21	Pennsylvania	261	16
Iowa	48	16	Rhode Island	4	1
Louisiana	1		South Dakota	19	4
Maine	3		Tennessee	7	
Maryland	25	3	Texas	14	2
Massachusetts	145	13	Utah	2	
Michigan	75	13	Vermont	24	3
Minnesota	101	12	Virginia	8	
Missouri	17	1	Washington	7	2
Nebraska	18	1	West Virginia	5	
New Jersey	35	6	Wisconsin	34	12

German, 259; Italian, 161; Hungarian, 36; American, 22; Negro, 14; Irish, 10; English and Irish, 5; Scotch, 5; Austrian, 4; Norwegian, 4; Foreign, 3; English, 2; Japanese, 1; Polish, 1; Syrian, 1; Turkish, 1; Greek, 1; Bohemian, 1; Danish, 1; Swedish, 1; Roumanian, 1; Canadian, 2.

Prevalence of Human Trichinosis. The disease is reportable and in the period up to 1914 there have been reported[4] 1550 cases with 240 deaths, a mortality of 16%. From 1909 to 1914 there were reported[4] 320 cases with 19 deaths, a 6% mortality. Probably the disease is much more prevalent, as mild cases escape recognition and perhaps even many severe ones go unrecognized. Table I, taken from B. H. Ransom's[4] report on trichinosis, shows the inci-

dence of the disease from 1842 to 1914 and the nationality of those affected, while Table II,* from the Bureau of Public Health, shows deaths in the United States from 1921 to 1929. Mancusi-Ungaro[5] in 1929 reports 67 cases in his own practice in four years. Six thousand, three hundred and twenty-nine cases were reported in Germany from 1881 to 1898.[4] Some routine autopsy reports show an incidence of trichinosis as high as 14%. Williams in 505 autopsies found trichina in 5.3%. Seventy-five of these autopsies were upon the insane and 12% of these had the disease. Additional autopsy figures are presented in Table III, taken from Ransom's article.[4]

TABLE II.—DEATHS FROM TRICHINOSIS IN THE REGISTRATION AREA OF THE U. S. Treasury Department, Bureau of Public Health, Washington, D. C.

	1921.	1922.	1923.	1924.	1925.	1926.	1927.	1928.	1929.
California	1	5	0	2	1	0	1	2	25
Colorado	0	0	0	1	0	0	0	0	0
Connecticut	1	0	0	0	1	0	1	1	14
Illinois	2	0	2	3	4	1	1	0	1
Indiana	0	0	0	1	0	0	0	0	0
Iowa	0	0	1	0	0	0	1	1	0
Kentucky	0	0	0	1	0	1	0	0	0
Maine	0	0	1	0	0	0	0	0	0
Maryland	0	0	1	0	0	0	0	0	0
Massachusetts	1	4	0	1	2	0	1	4	15
Michigan	0	0	1	0	0	0	0	0	0
Minnesota	0	0	0	0	2	2	0	0	0
Nebraska	0	0	0	1	0	0	0	1	0
New Jersey	2	1	0	0	3	0	0	2	4
New York	1	2	1	7	8	1	2	7	1
North Dakota	0	0	0	0	0	1	0	0	0
Ohio	1	2	0	3	0	0	0	2	13
Pennsylvania	2	0	0	0	0	0	0	1	12
South Carolina	0	0	0	1	0	0	0	0	0
Tennessee	0	0	0	0	0	1	1	0	0
Utah	0	0	0	1	0	0	0	0	0
Wisconsin	0	0	0	0	1	0	0	0	0
Georgia	..	..	..	..	..	..	..	..	3
South Dakota	..	..	..	..	..	..	..	..	10
Washington	..	..	..	..	..	..	..	..	1
Total registration area	11	14	7	22	22	7	8	21	85

States not named either had no deaths registered as due to trichinosis or were not in the Registration Area.

Cases of trichinosis are not reportable in many of the States and many cases are not reported even in States which have made it reportable by law. The reports are fragmentary and do not give an index of the true prevalence of the disease.

It is interesting to note that most cases as seen in this country, occur among foreigners because of their dietary habits. All of my 28 cases except one were Italian.

Prevalence of Porcine Trichinosis. Blumer[1] states that 6% of American hogs have the disease. From 1898 to 1906 when government inspection of hogs for export was required, 8,000,000 hogs were examined microscopically, 1.41% contained trichina and 1.16%

* Compiled for the author by the Bureau of Public Health Treasury Department, Washington, D. C.

had trichina-like bodies or disintegrating trichina, or one hog in every 39 had the disease.

TABLE III.—CASES OF HUMAN TRICHINOSIS FOUND AT AUTOPSIES.

Reporter.	Place.	Number of autopsies.	Number infested.	%
Glazier,	1881—New York, N. Y.	150	3	2
Glazier,	1881—Newark, N. J.	100	1	1.0
Glazier,	1881—Philadelphia, Pa.	40	1	2.5
Glazier,	1881—University of Virginia . . .	150	1	0.67
Glazier,	1881—San Francisco, Calif. . . .	13	0	...
Williams,	1901—Buffalo, N. Y., Phila., Pa., Baltimore, Md., Denver, Colo.	505	27	5.34
Osler,	1898—Baltimore, Md. and elsewhere	1000	6	0.6
Simmonds,	1910—St. Louis, Mo.	100	2	2.0
Whelpley,	1891—St. Louis, Mo.	20	1	5.0
Thornbury,	1894—Buffalo, N. Y.	21	3	14.29

Pathology. There is an acute gastroenteritis as shown by a congested mucosa, small hemorrhages and minute areas of necrosis and ulceration with swollen lymph glands. The liver, heart and kidneys often show parenchymatous or fatty changes, and the spleen may be enlarged. There is often subcutaneous edema. There may be pulmonary congestion with or without bronchopneumonia. After the fifth week the small grayish spots can be seen in the muscles. During the acute process, evidence of the mechanical or toxic effect of the larvæ may be seen in the brain, heart, lungs, pancreas, and intestine as localized hemorrhage, necrosis, and inflammatory edema. There is an infiltration of endothelial cells, lymphocytes, polymorphonuclear cells, and eosinophils. Complete healing practically always occurs except in the muscles. Sensitization to the protein of the destroyed larvæ is perhaps a cause of the toxic reaction and may explain the most striking symptom—the facial edema. The larvæ have been found in the placenta, milk of nursing women, excised mammary gland, pleural fluid, spinal fluid of a child three months after recovery, but never in the urine and rarely in the feces.[2]

Symptoms. There is occasionally an acute gastroenteritis immediately following the eating of the pork. This is probably usually due to decomposition of the meat and not to the trichinæ, but may be a result of a heavy infestation. In five days to three weeks, probably on an average in two weeks, symptoms appear. It is most striking that some members of a family will be acutely ill, others have no symptoms, and yet blood counts show them all infested.

Fever, anorexia, headache, swollen face and aching muscles are the striking symptoms. Fever may range from 99° to 106°, is of the remittent type, and lasts from one day to nine, or ten weeks with a fall by lysis. There is usually a marked anemia and loss of weight. Vomiting, diarrhea, and cramps, or perhaps constipation and gaseous distention may occur. Occasionally there is a hemorrhage from the bowel. Evidence of muscular involvement may be lacking, or the

involvement may give rise to such severe pain that opiates are necessary, and around tendinous insertions there may be involvement enough to simulate an arthritis or even a paralysis. The gait at times is rather characteristic, with knees bent and shoulders stooped. The eyes are said to show both retinal and conjunctival hemorrhages. There may even be an optic neuritis while there is frequently a complaint of burning and ocular pain. The skin may show herpes, erythema, pruritus, or an abdominal maculopapular eruption resembling that of typhoid fever while the edema, which is usually present around the eyes, may be more extensive and involve other parts of the body. Cerebral symptoms can simulate meningitis, as the patient may be irrational, have a stiff neck and a positive Kernig sign. Bronchitis and bronchopneumonia are frequent.

Laboratory Findings. There is usually a leukocytosis, and it very roughly corresponds to the severity of the disease. In five to eight days after infestation, the eosinophilia, which was first described by Thayer and Brown[3] in 1897, appears. It varies from 10 to 80% and may last for years. The degree of eosinophilia does not depend on the severity of the infestation, as a patient with a mild or an overwhelming infestation may not show an eosinophilia. In the first two weeks of infestation, the larvæ may frequently be found in the blood by laking 10 cc. of blood in 100 cc. of 3% acetic acid, centrifuging and examining the sediment. The larvæ can also frequently be found in the spinal fluid as Lindy and Van Cott[1] discovered in 1914. The spinal fluid cell count is also increased at times.

Diagnosis. From a consideration of the race and habits of the individual, and the rather striking facial edema and muscular pains, one would suspect the disease. A blood count would confirm the diagnosis. It must be remembered, however, that in those with a mild or an overwhelming infection there may be no eosinophilia and the disease might simulate pneumonia, meningitis, arthritis, typhoid fever, frontal or maxillary sinusitis, or mumps.

Treatment. Treatment is symptomatic. Prompt and radical purgation had best be resorted to when a person complains of being ill after eating pork. Also when a diagnosis of trichiniasis is made it is best to begin treatment by purgation followed by a daily enema. (Adult worms are said to persist in the intestinal tract for from two to six weeks.) Salzer,[2] and others have reported favorably on the use of convalescent serum. Salzer claims convalescent serum to cause the disappearance of the eosinophilia in forty-eight hours, while normal serum, salt solution, and arsphenaminized serum gave no results. If animals were fed trichinous meat within twenty-four hours of the injection of serum they became mildly ill, but if fed later were completely protected. Also if fed infected meat mixed with immune serum, they were protected. Salzer reports

2 human cases with subsidence of temperature in a few hours after administration of serum, and 24 rabbits cured within twenty-four hours. Arsphenamin has been found ineffectual and perhaps dangerous. Roentgen ray and radium are found unsuccessful.

TABLE IV.—DATA ON 29 CASES.

Case.	Age.	Onset, 1930	Duration in days.	Headache, fever, facial edema and muscular pains.	Gastrointestinal symptoms diarrhea and cramps or constipation and gaseous distention.	Eosinophilia, %
1	29	?	..	Yes*	Yes	0
2	31	?	..	Yes	No	45
3	?	?	..	Yes	No	40
4	41	Feb. 4	21	Yes*	No	0
5	40	Feb. 18	30	Yes*	Slight	25
6	30	Feb. 20	28	Yes*	Slight	10
7	9	Feb. 16	5	Headache	No	41
8	8	No complaints	..	No	No	52
9	6	Feb. 20	7	Headache	No	20
10	4	Feb. 16	5	Headache	No	12
11	48	Mar. 2	28	Yes	No	46
12	20	No complaints	..	No	No	3
13	17	Feb. 26	17	Yes	Slight pain	20
14	36	Feb. 7	21	Yes	Slight	3
15	43	Feb. 14	7	Yes	No	16
16	10	Feb. 17	7	Yes	No	14
17	13	Feb. 17	7	Yes	No	36
18	11	Feb. 21	3	Yes	No	20
19	15	Feb. 14	4	Yes	No	32
20	35	Feb. 20	8	Yes*	Yes	42
21	19	Feb. 17	7	Yes	No	15
22	25	Feb. 17	7	Yes	No	36
23	32	Feb. 17	7	Yes	No	38
24	28	Feb. 22	12	Yes	No	48
25	26	Feb. 6	8	Only muscle pains	No	50
26	37	No complaints	..	No	No	56
27	38	Mar. 4	3	Only muscle pains	Yes	58
28	27	Feb. 21	7	Yes	Yes	22
29	38	Nov. 13, 1929	45	Yes	....	86–33

* Symptoms marked.

Laked blood was studied from Cases II, III, V, VI and XX, but larvæ were found only in blood of Case XX.

Muscle sections were made from Cases III, IV, VI, VII and XXVI, but the embryos found only in muscle from Cases III, IV and VII.

Public Health Considerations. To prevent human trichinosis it is necessary to prevent the eating of pork containing living trichinæ. To prevent the hogs becoming infested, the most important points are: (1) The destruction of carcasses of hogs which die on the farm in such a manner that other hogs cannot eat them; (2) prohibition of the feeding of slops containing pork scraps; (3) prohibition of the feeding of unsterilized waste from slaughter houses to hogs; (4) since hogs eat rats and mice, which are a possible source of

trouble, rats and mice should be exterminated; manure piles, where they breed, removed and dead rats and mice disposed of so hogs cannot eat them. To prevent infested pork from reaching the consumer is a difficult problem, as inspection of meat has been found too expensive and too ineffectual to be practical. Encysted larvæ are frequently missed by the microscopic examination, as may be shown by Germany's experience[3] where, from 1881 to 1898, there were 2042 cases of trichinosis caused by eating inspected pork, with 112 deaths.

All pork should be treated so that any encysted larvæ will be killed. Proper cooking will of course, destroy the larvæ. Ransom[4] has found, after an exhaustive study, that cold, 5° F. for twenty days will destroy the larvæ, or a temperature of 140° F. will destroy them. To protect the public, the government requires that all pork for raw consumption be treated by one of these methods. Smoking and curing will probably destroy the larvæ, but it is not safe to depend on these processes.

An important consideration in treating meat by cold, or by heat is to consider the length of time it will take the heat, or cold to penetrate to the center of the meat. It takes two and a half hours to raise the temperature in the center of a 15 pound ham from 25° C. to 58° C., maintaining a temperature of 85° C. in the water in which it is being cooked.

Case Reports. The essential data of the 29 cases on which this report is based are presented in Table IV. Twenty-seven of the 29 cases of this series had eaten meat from one farm, where 15 pigs were said to have died from pneumonia during the preceding three or four months. The parasite was demonstrated in meat eaten by each family. It would seem probable, therefore, that the pneumonia in these pigs was a secondary consideration, and that they probably died of trichinosis.

The first group, Cases I to XIII inclusive, consists of three families living in apartments in the same house, and one child of their next-door neighbor. Two of these families bought a pig together, and each took half of it. They began eating it January 20. The first one to become ill was probably (D. B.) Case IV, fourteen days after eating pork, though (Mrs. M.) Case I, may have been ill before him.

Case I.—(Mrs. M.), aged twenty-nine years, seen January 30, was pregnant three months, had been vomiting occasionally for one month, had abdominal pain ten days, diarrhea five days, incessant vomiting for several days. This patient was sent to the hospital where, after numerous intravenous injections of glucose, and after proctoclysis, she improved enough to take some food by mouth. She remained a puzzle to those studying her because of her slight fever, inability to eat and prostration. A Vincent's infection was discovered, and two weeks later joint pain and stiffness, thought to be an arthritis secondary to the Vincent's infection, developed. The stiffness and pain were so severe that motion was almost impossible. Mild temperature elevation persisted and the patient aborted. On February

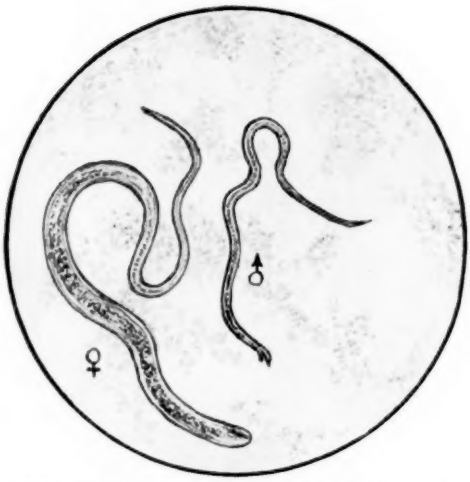

FIG. 1.—Male and female larvæ. (From Rivas' "Parasitology" with the author's permission.)

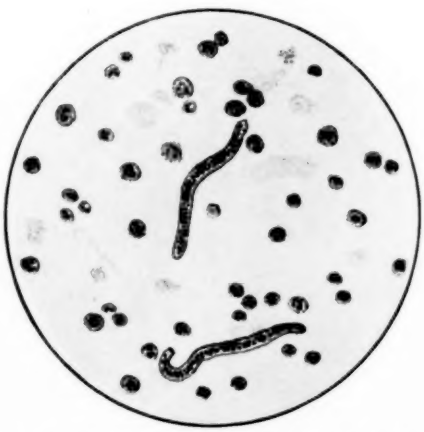

FIG. 2.—Larvæ in laked blood. (From Rivas' "Parasitology" with the author's permission.)

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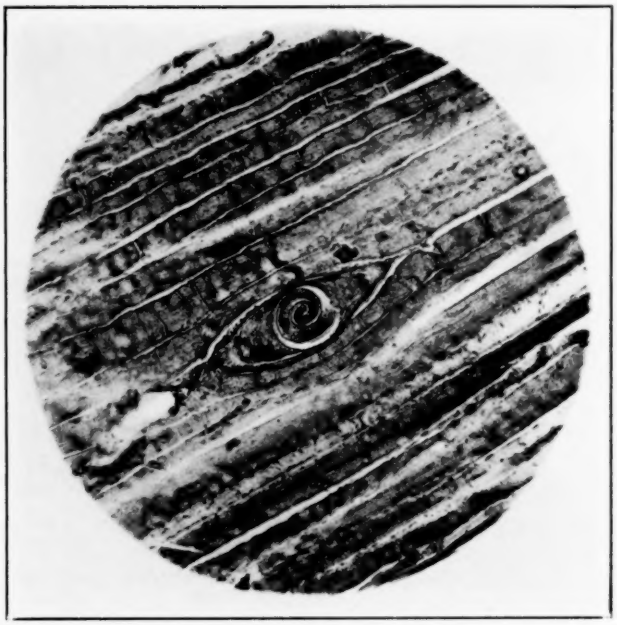

FIG. 3.—Encysted larvæ in pork.

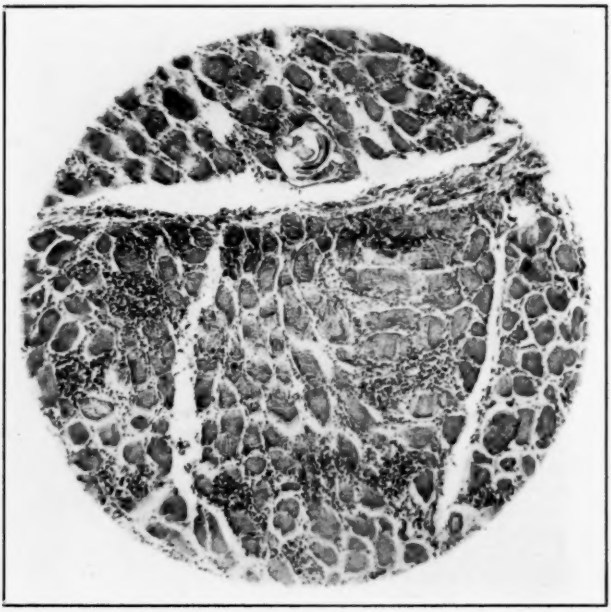

FIG. 4.—Low-power of human muscle showing encysted larvæ. Note giant cell.

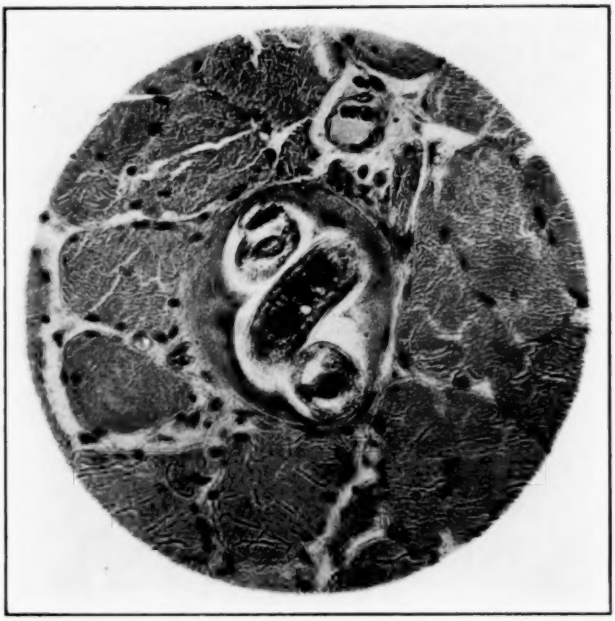

FIG. 5.—High-power human muscle showing encysted larvæ. (Note giant cell.)

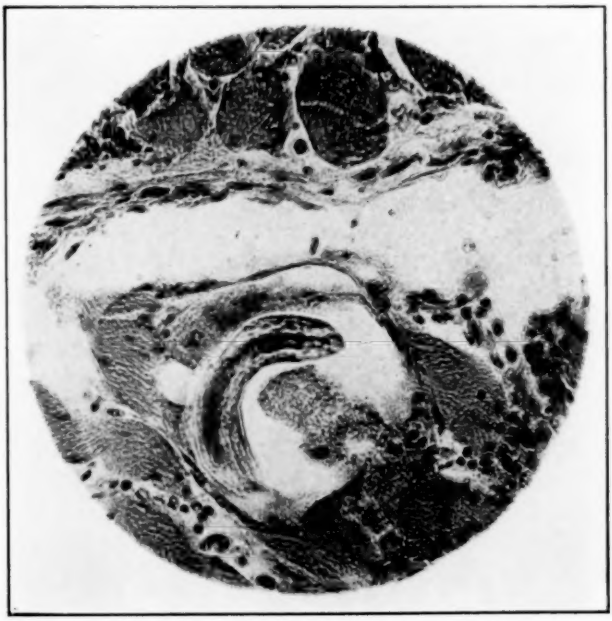

FIG. 6.—High-power human muscle showing encysted larvæ.

20, three weeks after admission, the patient died suddenly. The diagnosis was acute cardiac failure due to embolus, polyarthritis, abortion due to sepsis. The white blood count on February 6 was 5000 and on February 13, 9000. No eosinophils were present.

After her death, the death of Case IV, and the development of the disease in those who had eaten the pork, that is her family and the other occupants of the apartment house it became obvious that trichinosis was the undisputed cause of her death.

CASE II.—(M. M.), aged thirty-one years, onset about the first of February, had a severe infection with the usual symptoms. He was ill several weeks with severe muscular pains and a high eosinophilia but finally made an uneventful recovery.

CASE III.—(Baby M.), aged eight years, child of Case I, and Case II, in whose muscle the parasites were demonstrated, had a marked eosinophilia. Anemia necessitating transfusion developed also. She was treated at the Children's Hospital in Philadelphia.

CASE IV.—(D. B.), male, aged forty-one years, seen by the author on February 8, was a boarder in the household of Cases I and II. It was thought he had la grippe but his high temperature was so puzzling that the usual diagnostic laboratory tests for any questionable case were done. This man had a remarkable swelling of his masseter muscles. After determining that the extraordinary swelling was definitely muscular and had no connection with the parotid or lymphatic glands, the author dismissed consideration of it, thinking it just a muscular hypertrophy in a peasant's jaws. Because of the illness of others in the household, the patient was moved to another community. The doctor there thought because of his swollen face, that he had mumps. He later developed pneumonia and died. Autopsy showed the parasites in his muscles. The sections in illustration are from this autopsy. His leukocyte counts were 10,000 (3% eosinophils) on February 18, and 5800 (no eosinophils) on February 24.

CASE V.—(J. N.), male, aged forty years, the neighbor who bought the other half of the hog, became ill February 18 with the usual symptoms, almost a month after eating the first pork. He had mild diarrhea and cramps, was sick for one month, and was stiff and weak for several weeks thereafter, but made an absolute recovery.

CASE VI.—(Mrs. N.), aged thirty years, wife of Case V, became ill February 20 and was ill about three weeks with fever and muscular pains. Leukocyte counts ranged from 4200 to 4700. Muscle section soon after onset of the illness showed much inflammatory reaction, but no larvæ could be demonstrated. She also made a good recovery.

CASES VII and VIII.—(D. N.), male, aged nine years; (V. N.), male, aged eight years.

CASE IX.—(M. N.), male, aged six years, and CASE X (J. N., Jr.), male, aged four years, are children of Cases V and VI. They were studied because of the fact that children particularly (and adults to a lesser extent) may be infected and show no evidence of the disease. They were well and playing around, but 3 of the 4 had complained of slight headache for four or five days, and 2 of them were said to have had very slight edema around their eyes. White blood counts varied between 16,000 and 18,000, with eosino-

philia of 12 to 52%. Case VII (D. N.), male, aged nine years, had larvæ present in a biopsy specimen of muscle.

Case XI.—(Mrs. R. B.), aged forty-eight years, living in another apartment of the same house, was given one piece of sausage. On March 2, she became ill with fever and muscular pains, but was not very sick. The duration of illness was short, probably because of the small amount of pork eaten. The leukocyte count was 7000, eosinophils, 46%

Case XII.—(Mrs. R.), aged twenty years, living in another apartment, was studied because she ate the pork, though she had no complaints. She had an eosinophilia of 3% and probably had the disease.

Case XIII.—(Miss G. C.), aged seventeen years, a neighbor's child, was a frail, thin person who had a habit of getting up late and cooking her own breakfast. The family received some sausage as a gift from their neighbors (Cases V and VI), and all ate the meat without mishap, except Case XIII, who probably cooked her sausage inadequately. She first complained of headache February 26, but had no fever. Two days later fever developed. The leukocytes were 6000 to 8000, with at first 93% of neutrophils, on the sixth day there were 2% of eosinophils, on the ninth day 10%, on the fourteenth day 12%, and on the nineteenth day 20%. She had rather high fever and almost no muscular pains. Purgation and daily enemas probably helped prevent a more severe infestation.

Group II, Cases XIV to XXIII inclusive, consists of a family, their boarder, two sisters and a brother-in-law, who bought their pig from the same farm. Only two of this group, Cases XIV and XX, complained of active symptoms. The rest were studied because of the diagnosis established in Case XIV, the history of eating the same pork and a story of having had headache, swollen face, and muscular pains. Blood counts were made. Leukocyte counts ranged from 5000 to 20,000 with 14 to 42% of eosinophils.

Case XIV.—(Mrs. D. R.), aged thirty-six years, was in the hospital for a plastic operation when she developed headache, fever, muscular pains and swollen face. Various consultants saw her but no diagnosis was made until the day she left the hospital. The diagnosis was suggested because of these other cases, after she was practically well.

Case XV.—(D. D. R.), male, aged forty-three years, husband of Case XIV, became ill February 14, had a mild course with usual symptoms.

Case XVI.—(N. D.), male, aged ten years, son of Cases XIV and XV became ill on February 17. His symptoms were the usual ones and continued for one week.

Case XVII.—(J. D.), female, aged thirteen years, daughter of Cases XIV and XV, became mildly ill February 17 with usual symptoms but was ill for only one week.

Case XVIII.—(L. D.), female, aged eleven years, also daughter of Cases XIV and XV, became slightly ill February 21 and was ill only three days.

CASE XIX.—(E. D.), female, aged fifteen years, also daughter of Cases XIV and XV, became ill February 14 and was ill four days.

CASE XX.—(F. F.), male, aged thirty-five years, had severe muscular pains, fever and swollen face. Dr. Belk demonstrated the parasite in blood laked with acetic acid solution. This man became ill February 20, was in bed for four or five days, then limped painfully around for four or five more days when his muscular soreness disappeared.

CASE XXI.—(Mrs. M. E.), aged nineteen years, six months pregnant (sister-in-law of Case XV), had a mild infection and was in bed only a few days. Her pregnancy was not affected by this disease and she was delivered of a healthy child.

CASE XXII.—(L. E.), male, aged twenty-five years, husband of Case XXI, had a mild infection and was never in bed, in fact, had to be closely questioned to establish the fact that he had been ill.

CASE XXIII.—(Mrs. D.), aged thirty-two years, sister-in-law of Case XV, was never in bed but had a mild infection. She also had to be closely questioned to determine she had been ill.

Group III (Cases XXIV to XXVII inclusive) consists of another family and their "in-laws." They obtained their pork from the same farm. (Other members of this family were infected but were not studied, and, because confirmatory blood counts were not made, they are not included.) Interestingly, this group was discovered because the author heard by chance that the patients had been ill for several weeks with fever, swollen face, and muscular pains. The probability of trichinosis, suggested by telephone to the doctor treating them, was later confirmed by the other doctor.

CASE XXIV.—(Mr. D.), aged twenty-eight years, became ill February 22. He had exaggerated muscle pains requiring morphia but made an uneventful convalescence.

CASE XXV.—(Mrs. D.), aged twenty-six years, became ill February 26, but had only muscular pains, although rather severe ones.

CASE XXVI.—(Mrs. D.), aged thirty-seven years, a relative of Cases XXIV and XXV, was in the hospital for otitis media. A routine blood count showed an eosinophilia of 58%. She had no symptoms of trichinosis.

CASE XXVII.—(Mrs. M.), aged thirty-eight years, relative of Cases XXIV and XXV, became ill March 4 and was ill for only three days with muscular pains.

CASE XXVIII.—(P. R.), male, aged twenty-seven years, a relative of Group II, claims he had eaten no pork at their house but that he had the same symptoms. He had been eating pork elsewhere. He had 22% eosinophils.

CASE XXIX.—(Mr. H.), aged thirty-eight years, was seen in November, 1929, by Dr. J. L. Spangler. He complained only of fever and malaise.

He showed at first a high polymorphonuclear leukocytosis as did Case XIII, but later the typical eosinophilia, as will be seen in Table V:

TABLE V.—(CASE XXIX).

Day of disease.	White blood cells.	Neutrophil percentage.	Eosinophil percentage.
First	23,000	85	
Second	23,000	88	
Fourth	29,000	..	81
Sixth	27,000	..	51
Forty-second	23,000	..	72
One hundred and fiftieth	7,000	..	33

Discussion. It is interesting that an outbreak of trichinosis occurred in a community, traceable to one herd of infected hogs, and to note the family groups infected. Evidently the disease is becoming better recognized as one can see from the reports of the Bureau of Public Health at Washington.

In this outbreak the mildness and infrequency of gastrointestinal symptoms is noteworthy. The mortality was about 7% as compared to preceding mortality records of from 6 to 16%. Mortality records will, I feel sure, be low in carefully studied outbreaks where symptom-free infected individuals are included.

The author wishes to emphasize the importance of studying other members of the family of an infected individual (even in the absence of symptoms), the mild form the disease may take in children, the frequent errors of diagnosis even in the best hospitals, the prevalence of the disease among foreigners, the importance of blood counts in suspicious cases, the necessity of properly cooking pork, and the freedom from danger if it is properly cooked.

The striking clinical symptoms are repeated for emphasis: facial edema, muscular pains, headache and fever.

Summary. Twenty-nine cases of trichinosis are presented, occurring almost entirely among people of foreign birth, in a small community as a sporadic outbreak lasting twenty-seven days. All but 2 of these cases were infected by pork from a single farm where there was undoubtedly a local epidemic of the disease among the hogs during the winter. Trichinæ were demonstrated in numerous pieces of pork from this farm.

Two people died (7% mortality), 5 were acutely ill, 17 mildly ill, and 5 had practically no symptoms. Larvæ were searched for in laked blood of 5 patients and found in only 1 specimen. Three cases out of 5 studied showed encysted larvæ in muscle from biopsy. The characteristic eosinophilia was found in all cases except the 2 fatal ones.

Treatment for this disease is entirely symptomatic—except for an initial purgation, followed by enemas. Treatment with convalescent serum is promising.

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NEURASTHENIA AS A MANIFESTATION OF EMOTIONAL DISTURBANCES.

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Of the commoner problems that the practitioner encounters, the nervous patient is the most baffling. It is generally recognized that there is such a thing as psychogenesis—that mental mechanisms may produce symptoms resembling those of organic disease. But the physician, while accepting this abstractly, fails to integrate it in his mind as a significant part of his diagnostic outlook, largely because the nature of these mechanisms and of the forces activating them is only vaguely understood. A general idea persists that psychogenic ills are either malingered or imaginary. Symptoms such as tachycardia, fatigue, mucous colitis, seem too real to answer to such a tenuous explanation as "mind-stuff." The tendency is rather to seize upon any discoverable abnormality and ascribe all the trouble to it. One must examine the nervous case at least as thoroughly as any other. But when organic defects are revealed one must still be alert to question whether they are possible or sufficient causes for the symptoms. One must not be satisfied to diagnose neurasthenia simply because every other defect has been ruled out. The neuroses have their own more or less distinctive features and are not simply diagnoses reached by elimination of other possibilities.

Indeed organic ailments are frequently accompanied by some degree of psychoneurotic trouble and when the diagnosis is thus multiple it may require the greatest nicety of judgment to determine which of the symptoms are organic and which functional. Thus the young man with heart disease may suffer as much from apprehension of sudden death as he does from the lesion itself. Even the expert cardiologist will be at fault if he is unable to understand and treat the serious mental and physical responses to such a fear. This applies to every specialty, for it is far from unusual to

find that the patient's mental response to the fact of his illness is productive of a considerable fraction of the symptom picture. This, and the tremendous frequency of nervous disease make it impossible to relegate all such cases to the neuropsychiatrist's field. It is difficult to estimate accurately this frequency. It does not force itself upon our attention because it does not influence the mortality rate, but its morbidity rate must be tremendous.

The treatment of this great class of patients is a responsibility that rests chiefly with the general practitioner. It is he whom the patient first consults and it is he, by virtue of this early contact, who is best able to terminate many of the commoner, simpler types of neurosis. But after such a patient has passed from one physician to another with hope constantly deferred, with mind confused by conflicting opinions and with the original symptoms covered by an incrustation of secondary ones, the treatment becomes a task from which even the specialist may shrink.

Some understanding of psychogenesis is within the scope of every physician. Unfortunately the novice, without adequate preparation, too often attempts to absorb the literature of psychanalysis. For an empty stomach this is a rich and highly seasoned diet and it is not surprising that it is rejected. In the psychanalytic writings he finds much that he cannot understand, and of the remainder there is much that he cannot believe. He does not recognize the necessity for weighing critically every phase of a subject such as this which is so remote from ordinary experiential data that it can be expressed only in a language of its own invention or which, when it descends to the vernacular, assumes the privilege of interpreting words to fit its own needs. Thus the student is likely to discard the good of the psychanalytic theory along with the bad, with the vague feeling that there is something of the nature of a mystical revelation about it which the ordinary intelligence cannot hope to grasp.

The commoner cases of the neuroses may be interpreted without a knowledge of the vagaries of the erotic impulse and of their symbolic manifestations which is the basis of the psychanalytic method. One finds abundant data in the stresses of everyday life and in the mental and emotional responses with which we are equipped to meet them. These data are not the special tools of a single school of psychology but are a part of general biologic knowledge based largely upon experimental observation. Indeed, the work of Cannon upon the physical changes in various emotions and that of Pavlov upon the conditioned reflex are basic to this theory. The core of this conception is the biologic fact that definite alterations in function accompany emotional states. That palpitation, lump in the throat, flushing, pallor, tremor, dizziness, dyspnea, nausea, vomiting, faintness, sweating and importunate calls to bladder and bowel evacuation, may occur in emotional disturbance

is common knowledge, but the correlation of these with the symptoms of the neuroses is an important step toward an understanding of these ailments.

Such a theory of psychogenesis that is coherent with general life experience and with biology is more likely to be acceptable to many who find the orthodox psychanalytic approach to be so much a thing of its own kind, so isolated from other sciences, and thus so difficult to check against established scientific data that adherence to its tenets seems to imply a definite will-to-believe. This is not said with derogatory or controversial intent. Freud's great contribution in elucidating the rôle of repression and the dynamic subconscious with its bizarre influence upon conscious activity is the starting point as much for the biologic as for the psychanalytic theory. The latter, however, interprets neurotic symptoms chiefly as manifestations of "conversion." According to this conception, intolerable wishes and complexes that have been suppressed tend to enter consciousness surreptitiously under cover of a disguise (that is, the symptoms) which cloaks their repulsive content. This disguise is penetrable to the psychanalyst who interprets it as a symbol. Conversion applies more particularly to hysteria; the study of neurasthenia, confessedly incomplete, has led only to a wholly inadequate theory which ascribes it to masturbation.

The biologic school concerns itself chiefly with the neurasthenic response which it regards as an emotional reaction to depressing wishes and thoughts that have been suppressed because of their painful nature. That the emotion so frequently lags over in consciousness is the reason for the inadequacy of such suppression.

The present discussion is limited to neurasthenia. To define this neurosis on anything but an etiologic basis would be as difficult as to define typhoid fever without mentioning the typhoid bacillus. But as we are here dealing with etiology as a problem, it would be begging the question to classify on this basis. We must think, then, of neurasthenia in the sense of the "irritable weakness" of Beard—a state in which fatigue, irritability and symptoms resembling visceral disease are prominent, and in which there is a degree of suffering and anxiety not explainable by any obvious findings. Especially is it to be noted that hysteria and the miscellaneous neuroses are not included in the following:

In the study of emotional reactions we must first put aside the general impression that the emotion is the cause of the physical changes—palpitation, flushing, and so forth—which accompany it. In reality these physical changes are the direct results of the environmental stimulus and that which we term the emotion is the recognition that these changes are occurring. Thus we must not say that because we are afraid our heart beats quickly, we tremble and a lump arises in our throats, but we must say that when we feel these things we are in a state of fear. Likewise, anger does not cause the

head to throb and the muscles to grow tense, but rather the sensation attending these changes gives information that anger exists. If this seems absurd it is only because it is an unaccustomed viewpoint. Actually, this truth is inescapable. One cannot describe fear or anger except by listing the component physical changes, and each emotion is thus recognizable by its specific pattern of sensations.

The nature of these sensations is common knowledge. But it is desirable to consider the broad general meaning—the biologic purpose of these emotional manifestations. Fundamentally, and especially as we observe them in animals, they are of vital utility. As favorable or adverse changes occur in the environment the organism responds by a tendency to accept or reject them, to approach or avoid them, or to yield to or combat them. The physical changes that characterize emotions appear whenever the stimulus is such as to require a more vigorous motor response than usual. In the presence of danger there is an impulse to fight or flight. In the associated emotion of fear the circulation and respiration are speeded, the blood pressure is elevated, the neuromuscular mechanism is on edge with muscles tense and ready, and certain metabolic processes (for example, the mobilization of glycogen) are accelerated. These changes represent a readjustment of body processes to levels that will support the muscular system in attaining the maximum effectiveness for the violent motor outlay which the emergency demands. (Cannon has demonstrated this response to be a manifestation of suprarenal overaction.) Indeed there is a temporary subservience of all functions to that of motor action. There is an actual redistribution of blood, supplying an increased amount to the heart, lungs, and skeletal musculature at the expense of viscera (chiefly secretory and peristaltic), the function of which may be dispensed with for the moment.

Thus the palpitation, dyspnea, tremor, pallor, tenseness, peristaltic arrest, dry mouth, and so forth, which characterize fear are of utilitarian origin. It is probable that increased biologic insight will be able to discern a purposive element in other emotional phenomena where it is not at present obvious.* Thus the pilomotor activity ("gooseflesh") of fear would be meaningless if we did not recognize in it the vestiges of a mechanism whereby an animal may erect its fur that it may appear more formidable.

But this example has a further significance as an illustration of the general loss of utility of these responses as they occur in man. The reason is obvious. The things that frighten animals are grossly material—an enemy, the fall of a boulder, a cataclysm of nature. Moreover, animals, since they cannot forecast the future, react emotionally only to present perils. Against dangers such as these the fight-flight reaction is adequate.

* One must not confuse the picture by introducing instances of the "paralyzing" effect of fear, a condition produced by overwhelming danger with the obstruction of every possibility of escape.

Civilized man rarely encounters hazards of this kind. He reacts more to nonmaterial agents and to future dangers that he forsees. His dreads are of disease, poverty, disgrace, the supernatural, and —more subtly pervasive than all—his own faults and incapacities. Against such dangers a response that serves only to accelerate and intensify motor activity must be worthless. Nevertheless it persists. The utility that it possessed through long ages of primitive life has caused it to be formulated with a rigidity upon which the changed conditions of our own era have made not the slightest impression. That the response is the same whether we face a stock-market catastrophe, an armed highwayman, or the necessity of a serious surgical operation, is a measure of the emotional misfortune that we suffer. The very complexity and diverseness of our dangers have forced us to delay response until the most suitable course of action may be selected. It is in this that we have the basis of reason.

But if this response has largely fallen into a desuetude, it can hardly be called an innocuous one. One may think of it as a vestigial function comparable to certain vestigial organs which are not merely useless but are actually potential for harm. For the feeling of some degree of fear remains inseparable from every perception that even remotely suggests an injury to some aspect of our well-being. Moreover, it may be attached to anything, itself emotionally indifferent, that is associated (often merely by contiguity of place or time) with some dreadful or painful memory. *When such innocent associations recur in consciousness they may bear the whole burden of the emotional distress without the appearance of the real painful memory in consciousness.* This is a manifestation of the conditioned reflex as illustrated in Pavlov's experiments. After he had accustomed dogs to being fed at a definite interval after the ringing of a bell, Pavlov found that the secretion of digestive juices could be initiated (and at the appropriate interval) simply at the sound of the bell and without the exhibition of food. Here a physical reaction (comparable to that of emotion) was artificially attached (that is "conditioned") to an indifferent stimulus and was as readily evoked by it as by the natural stimulus of food.

Such a mechanism is at the basis of innumerable instances in both normal and neurotic where an emotion is felt in the apparent absence of an adequate cause. Intelligently introspective individuals by reviewing the circumstances surrounding such an occurrence can often recall a connection with some affect-bearing memory. A large part of the work of the psychopathologist is concerned with resynthesizing such associations. The following case is an example in point:

A young man displayed marked agitation accompanying a recent cough and upper chest pain. Examination revealed no lung pathology. It was learned that four years previously, when suffering from a cough, a physician had hesitantly informed him that there was *probably* nothing wrong with his lungs. This episode had been forgotten but was readily recalled upon

questioning. The patient was not conscious of a fear of tuberculosis but it seemed probable that his present cough had aroused a latent suspicion of that disease which the physician's remark had created. When this patient had been assured that there was really no disease of his lungs, his nervousness and indeed a large part of his pain disappeared.

Sometimes a stimulus, bearing a particular emotional tone by its own right, acquires an opposite one through association. This seems especially noticeable with odors. The celebrated chemist, encounters the stink peculiar to his laboratory with real delight because of its associative connection with the scene of his inspiration and triumphs. Again, to the nature-lover the smell of the skunk-cabbage in February is pleasant because it brings spring to his mind with a vividness far surpassing the more poetic harbingers.

Sexual vagaries present striking examples. There are cases where, even in marriage, an atmosphere of clandestinity is necessary for attaining the maximal erotic gratification. This, of course, is referable to escapades in earlier life of which the fear of detection was an inseparable feature. Impressions linked with early sexual episodes probably underlie many bizarre perversions and fetichisms.

The conditioning of responses explains the appearance of emotional manifestations (which, according to our theory, are identical with the symptoms of neurasthenia) in the absence of an obvious cause. Indeed, the neurotic does not recognize the emotion itself as a feature of his disease. The explanation is of some significance. First of all, the "feel" of anger or fear is a different thing from the intellectual formulation, "I am angry," or "I am afraid." The latter requires, in addition to the characteristic physical sensations, the recognition of some causal stimulus in the field of immediate experience. When this is present the physical sensations are not noticed individually but are interpreted collectively as a unit sensation, (that is, fear or anger) because innumerable experiences have taught us to evaluate them thus. But when the same somatic sensations appear without obvious cause there is no tendency to synthesize them into the consciousness of an emotional state and, being thus unexplainable, they command attention as unusual and are capable of being interpreted as evidence of an organic ailment.

Conversely, if the neurasthenic were to understand that his symptoms are essentially those of protracted fear, and if he were to discover a cause for such a fear he would automatically cease to regard himself as ill. The failure to recognize the cause for an emotion is due to several factors. It has been shown that our emotions, particularly fear, are seldom aroused by concrete things. The stimulus is often an unpleasant idea or complex of ideas only vaguely formulated. Such complexes may be so customary by reason of their long duration and so intangible by reason of their diffuseness as to be devoid of vividness. It is this very characteristic which enables them to permeate without detection the entire mental life with their

unhappy implication. They constitute the almost imperceptible but persistent, nagging emotional traumata that underlie so many deeply-seated neuroses. This is particularly descriptive of the inferiority complex. Nearly everyone possesses a feeling of relative unworthiness or incapacity. Ordinarily it acts as a spur to greater effort and is socially beneficial. But when grossly exaggerated it becomes a merciless goad, driving the sufferer to altogether inordinate exertions that he may combat his self-disesteem. It is well to note, when we are tempted to think of the neurasthenic as one of constitutionally inferior makeup, that much of the world's best work has resulted from an effort to conquer a feeling of self-dissatisfaction.

But the important fact is that such a self-estimation is so customary that it escapes conscious formulation. The tide of favorable circumstances may keep such a feeling submerged and impotent but a trifling discouragement or defeat often suffices to bring its emotive charge to the surface. The social snub that wounds so deeply does so not as a single affront but rather by arousing the emotion connected with a long series of forgotten doubts and fears. This is noteworthy in every sensitive individual, that the trivial unkindness which plunges them into such great unhappiness is thus potent chiefly because it revives and confirms the subject's own tendency to self-depreciation. A failure in some minor effort may likewise evoke the emotional depression of a complex that has been built up of all the failures and disappointments of a lifetime. It is like a spark that detonates a vast hidden storehouse.

The unit experiences in such a series may be too trivial, individually, to make a lasting impression on consciousness. Since the total complex is the abstract summation of these units, it is not surprising that it escapes recognition. It appears, then, that the position of a complex in the unconscious realm does not always depend on active repression.

Of course, such a complex is not necessarily the result of a slow accretion. Minerva-like, it may be born fully armed as a result of a single episode so agonizing in its implication that it must be forced out of mind if one is to attain mental peace. One tends to protect oneself against painful ideas by keeping them out of the field of attention. This, perhaps, is the essence of repression. For our present purpose it is not necessary to enter into the elaborate Freudian conception of this mechanism. It is simpler to think of repression as a wilful forgetting of an unpleasantness, a refusal to admit it into the field of attention, or a blind denial of its existence. The reaction to the fear of disease is a common example of this. Such fears as of syphilis, cancer, heart disease, are extremely prevalent and productive of much agitation and depression. It is a striking fact that the patient rarely divulges such a fear to his physician. It appears that he is himself only vaguely, if at all, aware of his fear. For example, the average well-informed young

man knows of the Wassermann test. But even though he may suffer an intense dread of syphilis he rarely requests a blood test or mentions anything that would suggest venereal disease. His complaints are likely to be miscellaneous odds and ends and the physician is led to suspect an underlying fear by the unusually severe affect that accompanies the rather trivial symptoms. It almost seems that the patient is trying to lead the physician away from the thought of venereal disease. In a sense, that is what he is trying to do—trying to lead the doctor to believe, as he has been trying to lead himself to believe, that he is suffering from overwork, kidney or heart disease, lack of vitamins, and so forth. If I may interpret the history of his fear I would say that the original fear of syphilis was quickly thrust out of mind with the self-assurance that it was impossible. He knows that he hasn't it and it is foolish to think any more about it. He devises innumerable reasons to prove its impossibility. Of course, this is all intellectualizing. The investigator becomes the more certain of the basic emotion in proportion to the patient's effort to disprove it.

Thus counter-ideas are erected so that the intolerable thought cannot enter consciousness. Unfortunately, the associated emotion may persist in consciousness but, as it is now detached from its stimulus, its true nature is not perceived. The physical changes characteristic of such an emotion are therefore misinterpreted as symptoms of organic disturbance.

So far, it has been our thesis that symptoms simulating organic diseases may be produced by protracted emotions, particularly fear. But neurasthenia presents other symptoms which do not bear this organic semblance and which are explainable on a somewhat different basis. These include the peculiar fatigue so characteristic of this neurosis and certain symptoms commonly recognized as "nervous"—confusion, irritability, lack of concentration, insomnia, poor memory, and so forth. To understand these we must abandon the word "fear" (hitherto employed for the sake of simplicity) and adopt the word "anxiety" as more accurately descriptive of the emotional state in neurasthenia. Anxiety implies fear but adds to it a connotation of uncertainty or doubt as to its validity. Fear is static—a response to some definite peril, anxiety fluctuates—the danger is at one moment terrifyingly real; at the next, only a foolish foreboding. Thus the man who receives an authoritative diagnosis of a heart lesion and a clear explanation of its prognosis will suffer fear, in contrast to the man who is repeatedly reminded by precordial pains that he *may* have heart trouble but who refuses to consult a physician to learn the truth. The former patient, however, grieved he may be, will not have the severe neurasthenia which the latter is likely to suffer. Such uncertainty invites a ceaseless mental struggle to disprove the existence of the thing dreaded in the face of repeated intimations of its reality.

"Worry" also implies uncertainty. But one worries about things the nature of which is understood, while one may be anxious without recognizing the cause for the emotion. Anxiety then is equivalent to fear with the modification of uncertainty and incomplete consciousness of the offending stimulus.

It is upon these elements of uncertainty and vagueness that the characteristic nervous symptoms appear to depend. Examples of the distress produced by uncertainty are innumerable—in mythology literature, history and everyday life. Wherever hope alternates repeatedly with despair, or fear with a sense of security, one notes this special type of suffering. The technique of torture nowhere achieves such perfection or refinement as where this form of mental pain is inflicted. It was the favorite tool of Torquemada. One thinks of such literary examples as the punishment of Tantalus (from which is derived the word "tantalize"), the ingenious vengeance of Morgan Le Fay in Mark Twain's "Connecticut Yankee" and most striking of all in its keen psychologic insight, Maupassant's story, "Useless Beauty." One may recall the well-known fact that during the war the soldiers suffered not so much from the fear of the enemy's attack as from the agonizing tension of awaiting the offensive that might begin the next minute or the next month. The effectiveness of the feint, both in war and with the pugilist, lies in the devastation which wearying uncertainty produces upon the morale of the opponent. Indeed one may make a general statement that suffering is never so unbearable as when it is prolonged and accentuated by the repeated access of hope.

In this connection we must refer, at least briefly, to the subject of mental conflict. All human activities and desires spring from an urge to gratify three major desires or instincts. These are concerned respectively with (1) our personal welfare, (2) reproduction and (3) the welfare of the social group to which we belong. Unhappily, the measures that would best serve any one of these aims is often at odds with the attainment of the other two. Thus there must be a continual curbing of each desire by the requirements of the others.

In this sense man serves three masters, or, to change the figure, he is harassed by the craving to possess both the penny and the cake. Frequently the decision cannot be readily made and the wavering impassé between alternatives constitutes the substance of conflict. It is to be emphasized that conflict is not a definite final obstruction to fulfillment of a desire. It is rather a state of indecision as to which craving is to be satisfied and which, abandoned. A frank failure of gratification is, of course, painful—an injury to ourselves (physical, financial, and so forth), the loss of a desired sexual goal, failure to conform as a unit of the herd (for example, "The Man Without a Country")—but, severe as such pain may be, it is of relatively short duration.

Conflict is capable of indefinite prolongation. This is a feature essential to the maintenance of a neurosis. Of course the struggle could be ended by abandoning either alternative but the prospect of a painful sacrifice usually leads one to defer such a step—especially since an uncertain hope deludes one into believing that it may perhaps be unnecessary. Moreover, where the elements of the conflict are not clearly formulated in consciousness they are not accessible to such direct handling. The function of the psychotherapist is chiefly to bring them vividly before the patient and often to show him that the sharp brief pain is easier to bear than the nagging distress of indecision. It is the realization of this which sometimes causes the hunted criminal to surrender himself that he may escape the prolonged threat against his freedom. The contrast between the two forms of suffering is like that between the sting of a bee and the harassing annoyance of a swarm of mosquitoes.

As a clinical example let us picture 2 hypothetic cases each presenting interference with sex desires. In the first an organic impotence, as from castration, develops. Once this has been accepted as an immutable fact there is a strong possibility of resignation, adjustment and even contentment. The second individual fails to gratify his erotic desires because it would necessitate sacrificing certain things that he cannot lightly put aside—his sense of moral integrity, his financial security, his job as a school teacher, his health (fear of venereal disease) and so forth. The mind of this man is likely to continue in a state of indecision, of tension, of uncertainty, until he can bring himself to abandon one or the other group of desires. This is typical of the usual conception of conflict—that is, of desire and counter-desire.

The word "conflict" may be conveniently extended, however, to include cases in which the prospect of gratification is potentially obstructed by something we dread without being entirely certain of its existence—that is, illness (physical, mental, sexual); occupational or social incapacities. As in true conflict, these dreads do not compel the abandonment of a goal but permit continued effort while fear of failure repeatedly alternates with optimism. Here there is a back-and-forth struggle between the poles of hope and discouragement while in classical conflict it is between opposed desires. (It is to be understood that "desires" includes the craving not merely for concrete things and activities but also for the attainment and retention of such things as health, prestige, self-esteem, and the like. The ordinary cases of neurosis more often depend upon reaction to threats against these things than upon the spectacular and unusual complexes which, because they are spectacular and unusual, occupy the more prominent place in the literature.)

The thought of being baffled in attaining such a desire produces, at least in miniature form, all the unpleasant emotional sensations that would accompany actual failure. When we consider the possi-

bility of interminable repetitions of such an emotional trauma, we can understand the reason for the protracted cat-and-mouse play of suffering in anxiety states.

The dilemma of uncertainty wages back and forth like a battle. The damage at any one moment is small; its devastating effect depends upon the prolonged, insidious bombardment of minute emotional injuries and the tremendous expenditure of mental effort upon the unavailing struggle. This accounts in part for the exhaustion that is so prominent in neurasthenia. But there are other reasons for this fatigue. In any effort the associated interest or advantage is very potent in lessening the weariness. The neurasthenic, however, has very little interest in ordinary activities. The warring elements of the conflict so completely usurp the focus of attention that all else is relegated to the periphery. The routine of the day—"dreary, flat, stale and unprofitable"—is approached as something that somehow or other must be gotten over with. This perhaps explains the greater depression in the morning or at the beginning of a task.

Certainly, this is not physical fatigue. The patient may become intensely tired with one type of work while another, demanding many times the energy output, occasions no discomfort. Such "selective" fatigue is likely to occur when the work is at variance with the worker's tastes or ambitions. This is a common conflict—economic necessity versus the desire for a more dignified or pleasing occupation. There are other cases where, although the work is pleasing, the worker fears that he may be incapable of succeeding. With such lack of confidence he dreads to make any trial lest failure should confirm his doubts. Such people seem to prefer a state of anxious ignorance to one of certainty.

Occasionally some special experience may have unpleasantly conditioned an activity.

A woman complained of rapid exhaustion whenever she attempted to walk or to talk. Some months previously she had learned that she had hypertension. In her mind this amounted to a threat of apoplexy and any exertion or excitement might precipitate this mishap. Of course, these facts were not mentioned spontaneously. The intolerable thought of a stroke had been quickly suppressed but the association of this with physical exertion (that is, walking) and with excitement (that is, conversation) had caused the emotion to be attached to these activities. This fear was manifested as fatigue. It is interesting to note that this woman, who tired almost immediately in social conversation, was able to talk uninterruptedly for one-half hour (I timed her) while describing her symptoms.

Anyone is likely to grow disinterested and tired in an effort that does not offer a reasonable prospect of being successful. The most fatiguing task that I encounter is the treatment of a certain hysterical patient who, I feel, is determined not to be relieved (deprived?) of her symptoms.

Generalizing then: such a fatigue is really the expression in consciousness of a lack of desire for an activity or a positive distaste or fear of it. To fear to do a thing is to wish not to do it, and to be indifferent or uninterested is only a lesser degree of the same disinclination. It is significant that the words "tiresome" and "wearisome" have come to mean "boring" and "uninteresting."

For explanation of other nervous symptoms we may likewise refer to anxiety with its conflict of mutually obstructive desires or its futile interplay of hopes and fears, and to the manner in which it usurps the center of attention. It almost seems a paradox to say that one is not fully conscious of a disturbance which so fills this field. But, to take as an example a person influenced by a broad inferiority feeling, we find that the feeling itself is not expressed in consciousness because it has been buried beneath a mass of counter-ideas. The subject is constantly and avidly seizing upon every incident that will raise his self-esteem and is striving to turn his back upon everything that might arouse the intolerable self-dissatisfaction. It is this effort to establish his personal worth that most strikingly identifies the sufferer of the inferiority complex. A setback, a mere word of discouragement may suffice to re-animate this complex in its shallow grave and the sufferer must again accumulate every shred of evidence of his superiority to escape the torment. With such an individual the struggle may be endless and the very core of his mental life may be the scene of repeatedly frustrated efforts to lay a ghost. With this as the only thing of real importance, it is not surprising that there should be a loss of interest in other matters. A host of symptoms take origin from this. Without interest there is difficulty in concentrating the attention. Since we remember things in proportion to the degree with which we give them our undivided attention, the poor memory of neurasthenia follows as a corollary.

Likewise, where the sphere of interest is so constricted there must occur a tendency to withdrawal from externals and from social contacts. Here, however, there may be a more specific factor—the self-protective avoidance of any contact with the environment in which there is possibility of defeat.

The irritability of the neurasthenic is the same as the response of the animal or child that is teased or of any of us when repeatedly frustrated. It is curious that the reaction seems to bear little proportional relation to the importance of the obstructed effort. The cross-word puzzle and the game of solitaire that come just short of solution, the ligature that repeatedly slips, the columns of figures that persistently refuse to balance, the street noises that prevent our concentrating, all produce a markedly disagreeable mood. Many will experience under such conditions a peculiar head discomfort, confusion, and a tremulous muscle tenseness. We must also remember, among the causes of this irritability, the

childish tendency to shift to the outside world the blame for inner distress and dissatisfaction. The onlooker at the card game annoys us but never so much as when the game is going unfavorably. Anyone, introspecting honestly, will occasionally detect himself in the act of "kicking the cat." We feel that if other people are not to blame they somehow ought to be.

The mental confusion and turmoil are the experience of anyone who is repeatedly frustrated. The indecision that characterizes anxiety is essentially such a frustration. The fact that the elements of the conflict are not recognized does not clarify the mental response. One does not "halt between two opinions." One chases back and forth without achieving a decision until the baffling futility of the effort renders all activity frantic and incoherent and formless. The "headache" and unusual head sensations are recognized by many normal people as concomitant to stress and anxiety. This is typified by the "stock-market headache."

The cause of the tremor is manifold. The phase significant at this point is that a perverted emotional response—the motor set of tense, expectant readiness for a biologic defence reaction but illustrating in its very unsteadiness the uncertainty of the stimulus that evokes it.

It would be presumptuous to try to explain all the manifestations of neurasthenia. Here the attempt has been to indicate that the more characteristic symptoms may be accounted for on a purely psychogenic basis and through the agency of mental mechanisms that are relatively simple.

Summary. The foregoing discussion attempts to explain neurasthenia as the emotional reaction of anxiety. Conceiving anxiety to be fear plus an element of uncertainty, we find that those symptoms referable to functional visceral disturbances correspond closely to the normal biologic response in fear states. Since in the neurasthenic the cause for such fear is subconscious, the true nature of these visceral sensations is not understood and they are interpreted as symptoms of disease. Moreover, the patient is unable to dispose of such subconscious fears by rational handling and the neurosis is thereby perpetuated.

The attendant uncertainty gives rise to a ceaseless mental struggle to solve a problem, even the nature of which is not clearly known. This futile back-and-forth play of thought preëmpts the field of attention and renders all else unimportant and without interest. The disinclination for ordinary activities is interpreted as fatigue, while the intellectual disinterest leads to failure of concentration, and hence of memory. Tremor and restlessness are the motor manifestations of uncertainty of purpose and lack of mental repose. Such manifestations are felt as transient episodes by normal people when facing, consciously, a complicated or baffling problem. It is only when the cause for these disturbances is unknown that they are interpreted as abnormal.

THE NITROGEN BALANCE DURING DIETARY CORRECTION OF OBESITY.

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In the dietary treatment of obesity as described by Strang, McClugage and Evans,[1] a markedly deficient caloric intake was maintained for months without clinical evidence of starvation. In the planning of this diet, thought was directed toward the administration of the protein requirements of the body in order to avoid the depression of metabolism which accompanies a lowering of the nitrogen exchange. The nitrogen studies which were made during the reduction of 5 patients, each more than 70 per cent above the ideal weight at the beginning are described in this paper.

Methods.—The patients were studied under the rigid technique of the metabolic division of the hospital for from forty-three to two hundred and sixty-five days. The periods of observation are divided into: (1) Preliminary; (2) low carbohydrate; (3) increased carbohydrate. During the preliminary period the patients ate as they wished. The reduction period was divided into the low carbohydrate, in which the least possible carbohydrate was given, and the final period, in which the carbohydrate was increased by approximately 20 gm.

The nitrogen intake was calculated from the food tables of Atwater and Bryant.[2] The nitrogen output of the urine was determined on a portion of the total mixed specimens of a week. The figures recorded represent the total nitrogen of the mixture divided by the number of days, that is, the average daily nitrogen for the designated period. The nitrogen content was determined by the macro-Kjeldahl method on duplicate 5-cc. samples in all cases except for the first seven weeks on Patient 4 and the first ten weeks on Patient 5. In these 2 instances micro-Kjeldahl determinations were done in duplicate on 1 cc. of a 1 to 20 dilution of the daily urines, and the recorded values are the averages of the daily determinations for the respective periods. Short periods are present in Cases 1, 4 and 5, for which the urine values are not available.

The feces nitrogen was found by the macro-Kjeldahl method upon

aliquot portions of the mixed stool for each week on Patients 1, 2 and 3. On Patients 4 and 5 analyses were performed upon only two representative weeks. We have used arbitrarily the value of 1 gm. nitrogen per day throughout on both of these cases because this value appears reasonable in view of the analyses made and in view of the detailed observation made upon the other patients. The error thus introduced is relatively small and tends to increase slightly the figures for the total nitrogen output.

Results. *Preliminary Period.* During the preliminary period, in which 4 patients were observed for an average of five days, the freely selected intake averaged 69 gm. of protein, 235 gm. of carbohydrate and 128 gm. of fat. It will be noted that of the 2400 calories ingested, 11 per cent came from protein, 39 per cent from carbohydrate and 50 per cent from fat. For each gram of protein there were 3.4 gm. of carbohydrate. The protein fraction corresponds to approximately 0.4 gm. of protein per kg. of the actual weight of the patients. However, on the basis of ideal weight, 69 gm. represents 1 gm. per kg. The nitrogen content of the diet as estimated from the food tables is 11.1 gm. per day. The data are summarized in Table I.

The total nitrogen output averaged 10.9 gm. a day when the estimated value for the feces nitrogen of 2 patients is included. Patient 4 showed the only marked variation from the average output. However, the inclusion of this output, 14 gm. per day, elevates the average by only 10 per cent.

The average figures for nitrogen equilibrium suggest that these patients were on the whole nearly in nitrogen balance. The period of observation, five days, was too short for the mergence of the daily swings of intake and output into consistent averages. Patient 4, for example, appears to have lost 3.7 gm. of nitrogen per day for six days, while Patient 5 gained 5.2 gm. per day for four days. These extreme values would probably have leveled off in longer periods of observation. All of the patients lost weight in this period, which indicates a submaintenance caloric value of the diet. The approximate correspondence between the nitrogen intake and output shows that protein tissues were not lost.

The level of nitrogen metabolism which was observed in these patients falls well within the limits which have been reported for normal persons. Denis and Borgstrom[3] found a total protein metabolism of approximately 1.1 gm. per kg. of body weight, or 0.17 gm. of nitrogen per kg. in 233 normal young males. Beard,[4] obtained almost identical figures from 400 analyses. Our patients, who were securing a slightly submaintenance diet, were operating at a level of 0.064 gm. of nitrogen per kg. of actual weight, which is, however, 0.16 gm. per kg. of ideal weight. These observations indicate that there is no fundamental depression of protein metabolism which is characteristic of obesity.

TABLE I.—AVERAGE DAILY NITROGEN EXCHANGE. PRELIMINARY PERIOD.

Case.	Age.	Days.	Weight.					Intake.					Nitrogen output.			Nitrogen balance, gm.	Nitrogen per kg. actual weight.	Nitrogen per kg. ideal weight.
			Initial, kg.	Ideal, kg.	Excess, per cent.	Average for period, kg.	Final, kg.	Calories.	Protein, gm.	Carbohydrate, gm.	Fat, gm.	Nitrogen, gm.	Urine, gm.	Feces, gm.	Total, gm.			
1	37	7	171.6	61.2	180	170.3	170.0	1894	58	183	100	9.3	7.9	1.9	9.8	−0.5	0.058	0.16
2	45	0	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
3	53	6	145.3	67.1	116	145.5	145.0	1833	57	178	96	9.1	8.1	1.3	9.4	−0.3	0.064	0.14
4	58	6	194.2	70.9	174	193.7	193.2	2122	64	227	103	10.3	13.0	1.0*	14.0	−3.7	0.071	0.20
5	60	4	163.1	64.5	152	162.8	160.6	3762	98	352	211	15.7	9.5	1.0*	10.5	+5.2	0.064	0.16
Average	51	5	168.5	65.9	155	168.1	167.2	2403	69	235	128	11.1	9.6	1.3	10.9	+0.2	0.064	0.16

* Estimated.

TABLE II.—AVERAGE DAILY NITROGEN EXCHANGE. LOW CARBOHYDRATE PERIOD.

Case.	Days.	Weight.				Intake.					Nitrogen output.			Nitrogen balance, gm.	Nitrogen per kg. actual weight.	Nitrogen per kg. ideal weight.
		Initial, kg.	Ideal, kg.	Excess, per cent.	Average for period, kg.	Final, kg.	Calories.	Protein, gm.	Carbohydrate gm.	Fat, gm.	Nitrogen, gm.	Urine, gm.	Feces, gm.	Total, gm.			
1	58	170.0	61.2	178	157.3	148.0	330	53	11	8	8.5	9.4	0.4	9.8	−1.3	0.062	0.16
2	43	113.1	65.9	71	109.0	104.0	380	63	11	9	10.0	13.4	0.6	14.0	−4.0	0.120	0.21
3	0	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
4	37	193.2	70.9	172	185.2	178.6	325	65	7	4	10.4	10.6	1.0*	11.6	−1.2	0.062	0.16
5	57	160.6	64.5	149	151.7	143.2	308	53	10	6	8.5	9.1	1.0*	10.1	−1.6	0.065	0.16
Average	39	159.2	65.6	142	150.8	143.5	336	59	10	7	9.4	10.6	0.8	11.4	−2.0	0.077	0.17

* Estimated.

Low Carbohydrate Period. During the second period of observation, which lasted thirty-nine days, the diet which was ordered provided 66 gm. of protein but no carbohydrate or fat other than that which was inseparable from the protein or vitamin ration. The actual diet eaten averaged 59 gm. of protein, 10 gm. of carbohydrate and 7 gm. of fat. The total caloric value was 336 calories, of

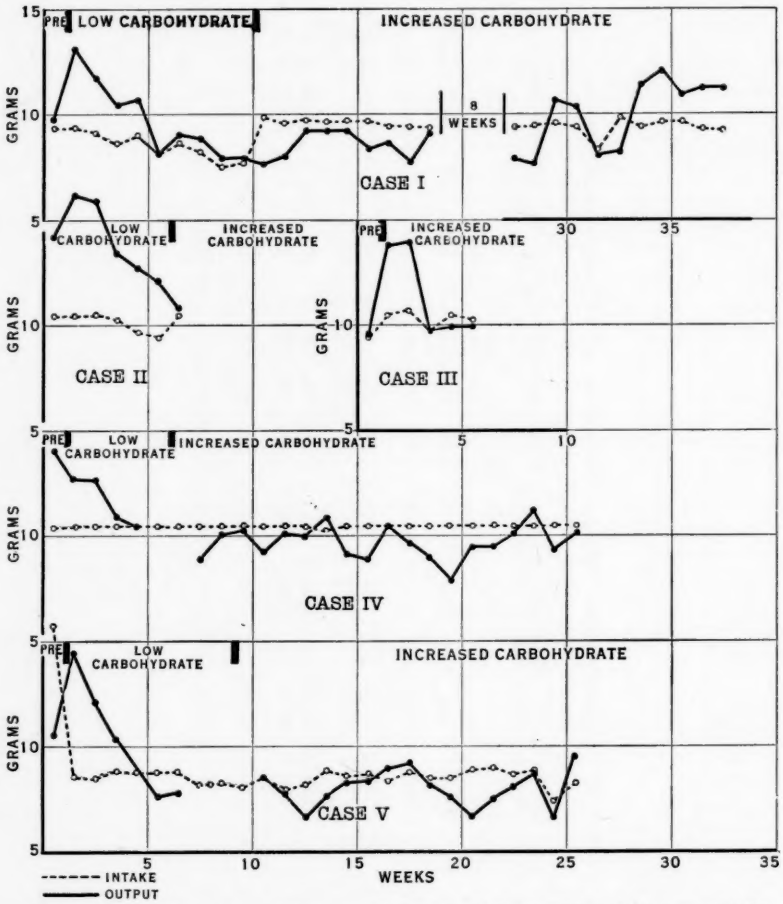

CHART I.—Average daily nitrogen exchange recorded by weeks of dietary periods.

which 70 per cent were given as protein and only 12 per cent as carbohydrate. For each gram of protein there was but $\frac{1}{6}$ gm. of carbohydrate. The slight depression of the ingested protein below that desired is attributable to the fact that none of the patients was able to eat the entire protein ration after the first few weeks. The 59 gm., however, corresponds to slightly less than 0.4 gm. of protein per kg. of actual weight, but to 0.9 gm. per kg. of ideal

weight. The estimated nitrogen content is 9.4 gm. Table II summarizes the data of this period.

The output of nitrogen averaged 11.4 gm. per day for the entire period. It will be noted from the observations for the weekly periods which are detailed in Table III and plotted in Chart I, that the output was not uniform throughout the dietary period. During the first three weeks, in one case six weeks, the output is greatly increased. In general, there is a tendency toward a marked preliminary increase in output which is followed by a return to almost the original level.

During the second period all of the patients were in negative nitrogen balance. The average loss was 2.0 gm. per day. A portion of the loss is due to a decrease in nitrogen intake. In fact, in Patient 1 the negative balance during the last five weeks is attributable almost entirely to this factor. The principal feature, however, is the excessive output early in the period. Losses of 3 to 6 gm. a day are characteristic of the first two weeks, following which the output remained but slightly above the intake. Patient 2 lost more than 2.5 gm. for six weeks, with a maximum loss of 5.7 gm. per day in the second week. In Patients 4 and 5 the output fell below the intake after the fourth week, thus producing a positive balance.

The average level of nitrogen metabolism, 0.17 gm. per kg. of ideal weight, is but slightly above the corresponding figure for the preliminary period. The ratio of nitrogen output to ideal weight is used in preference to that for actual weight, as it provides a better basis for comparison of the different periods. The ratio of nitrogen exchange to kilograms of actual weight for this period is 0.077. In view of the continuous loss of weight, this figure is based upon the average weight for the period. The numerical increase as compared to the corresponding figure for the earlier period, 0.013, is due to the diminution in weight as well as to the slight rise in nitrogen level. In the early weeks, however, the nitrogen level was considerably elevated, the maximum observations being in Patient 2, whose average output for six weeks was 0.21 gm. per kg. of ideal weight with the highest value, 0.24, in the second week. Following the initial elevation of nitrogen level, all cases showed a return to approximately the initial level. In only 2 cases was it significantly depressed.

Increased Carbohydrate Period.—The final period of dieting, averaging one hundred and one days, was characterized by the addition of approximately 20 gm. of carbohydrate to the diet. The figures for actual intake were protein, 61 gm., carbohydrate, 29 gm., and fat, 9 gm. Of the total calories, 444, only 55 per cent were now derived from protein, while 26 per cent were from carbohydrate. The increase in carbohydrate changed the ratio of carbohydrate to protein to ½ gm. of carbohydrate per gm. of protein. The greater

TABLE III.—AVERAGE DAILY NITROGEN EXCHANGE RECORDED BY WEEKS OF DIETARY PERIODS.

	Week.	Case I.			Case II.			Case III.			Case IV.			Case V.		
		Int., gm.	Out., gm.	Diff., gm.	Int., gm.	Out., gm.	Diff., gm.	Int., gm.	Out., gm.	Diff., gm.	Int., gm.	Out., gm.	Diff., gm.	Int., gm.	Out., gm.	Diff., gm.
Preliminary period	1	9.3	9.8	−0.5	..	..	..	9.5	9.4	0.1	10.3	14.0	−3.7	15.7	10.5	5.2
	2															
Low carbohydrate period	1	9.4	13.2	−3.8	10.4	14.1	−3.7	..	..	..	10.4	12.7	−2.3	8.5	14.3	−5.8
	2	9.1	11.8	−2.7	10.4	16.1	−5.7	..	..	..	10.4	12.6	−2.2	8.5	12.0	−3.5
	3	8.6	10.5	−1.9	10.4	15.8	−5.4	..	..	..	10.4	10.9	−0.5	8.8	10.2	−1.4
	4	9.0	10.6	−1.6	10.1	13.4	−3.3	..	..	..	10.4	10.4	0.0	8.8	9.0	−0.2
	5	8.1	8.2	−0.1	9.5	12.7	−3.2	..	..	..	10.4	..	..	8.8	7.6	1.2
	6	8.6	9.0	−0.4	9.4	12.0	−2.6	..	..	..	..	..	..	8.8	7.8	1.0
	7	8.2	8.9	−0.7	..	..	..	..	..	..	..	..	..	8.2		
	8	7.5	7.9	−0.4	..	..	..	..	..	..	..	..	..	8.3		
	9	7.8	7.9	−0.1												
Increased carbohydrate period	1	9.9	7.6	2.3	10.3	10.7	−0.4	10.4	13.7	−3.3	10.4	..	..	8.0		
	2	9.5	8.0	1.5	..	..	..	10.6	13.8	−3.2	10.4	8.7	1.7	8.5	8.5	0.0
	3	9.7	9.2	0.5	..	..	..	9.6	9.7	−0.1	10.4	10.0	0.4	7.8	7.7	0.1
	4	9.6	9.2	0.4	..	..	..	10.4	9.9	0.5	10.4	10.1	0.3	8.2	6.6	1.6
	5	9.6	9.2	0.4	..	..	..	10.1	9.9	0.2	10.4	9.2	1.2	8.8	7.6	1.2
	6	9.6	8.4	1.2	..	..	..	..	..	..	10.4	10.0	0.4	8.6	8.2	0.4
	7	9.4	8.6	0.8	..	..	..	..	..	..	10.4	9.9	0.5	8.7	8.3	0.4
	8	9.4	7.7	1.7	..	..	..	..	..	..	10.1	10.9	−0.8	8.3	8.9	−0.6
	9	9.3	9.1	0.2	..	..	..	..	..	..	10.4	9.0	1.4	8.7	9.1	−0.4
	10	..	..	..	..	..	..	..	..	..	10.4	8.7	1.7	8.5	8.0	0.5
	11	..	..	..	..	..	..	..	..	..	10.4	10.3	0.1	8.5	7.5	1.0
	12	..	..	..	..	..	..	..	..	..	10.4	9.5	0.9	8.8	6.6	2.2
	13	..	..	..	..	..	..	..	..	..	10.4	8.9	1.5	8.9	7.5	1.4
	14	..	..	..	..	..	..	..	..	..	10.4	7.9	2.5	8.6	8.0	0.6
	15	..	..	..	..	..	..	..	..	..	10.4	9.4	1.0	8.7	8.6	0.1
	16	..	..	..	..	..	..	..	..	..	10.4	9.4	1.0	7.4	6.6	0.8
	17	..	..	..	..	..	..	..	..	..	10.4	10.0	0.4	8.2	9.5	−1.3
	18	9.4	7.9	1.5	..	..	..	..	..	..	10.4	11.2	−0.8			
	19	9.4	7.6	1.8	..	..	..	..	..	..	10.4	9.2	1.2			
	20	9.6	10.7	−1.1	..	..	..	..	..	..	10.4	10.0	0.4			
	21	9.4	10.4	−1.0												
	22	8.3	8.0	0.3												
	23	9.8	8.2	1.6												
	24	9.4	11.5	−2.1												
	25	9.6	12.1	−2.5												
	26	9.6	11.0	−1.4												
	27	9.3	11.3	−2.0												
	28	9.3	11.3	−2.0												

palatability of this menu enabled the patients to approach more nearly the desired 66 gm. of protein or 1 gm. per kg. Due to the lowered average actual weight of this period, the ratio of protein to kilograms of actual weight becomes 0.5, while the ratio based upon ideal weight remains slightly above 0.9. The calculated nitrogen content of this diet was 9.7 gm. per day. The summary of the data for this period appears in Table IV.

The nitrogen output averaged 9.8 gm. per day for the entire period. Attention should be called to the use of the value 1 gm. for the estimated fecal nitrogen for the entire period in Patients 4 and 5. This is undoubtedly a maximum value, but places the probable error in the direction of a nitrogen loss. The dependent statements regarding nitrogen balance are, therefore, conservative. As in the low carbohydrate period, the nitrogen output was not uniform from week to week, variations as great as 3 gm. per day being noted between successive weeks. (See Table III and Chart I.) A suggestively cyclic character of these fluctuations appears in those having a prolonged stay, Patients 1, 4 and 5. It is important, however, that the average nitrogen output did not drop appreciably after one hundred and twenty to two hundred days on 450-calorie diets.

The balance between intake and output in the third period was maintained in a most unexpected degree. For one hundred and one days there was an average loss of only 0.1 gm. a day. The purposeful use of 1 gm. for the feces nitrogen equivalent in Patients 4 and 5 is responsible to a large extent for this apparent loss. A phenomenon which was observed repeatedly on each of the long term patients is the apparent storage of nitrogen for periods of two to eight weeks, during which the patients consistently lost weight. The remarkable constancy of the nitrogen intake emphasizes that these fluctuations in balance depend upon variations in output. In spite of the fluctuations from week to week, it is worthy of emphasis that the figures for the entire period show but slight loss. In fact, these patients lost certainly less than 10 gm. of nitrogen in three months while at the same time they lost 21.6 kg. in weight. In view of the marked loss of nitrogen which was observed in each patient at the outset of the low carbohydrate régime, an attempt was made on one patient, No. 3, to avoid this loss by passing directly from the preliminary period to the increased carbohydrate period. Nitrogen loss was not prevented, but the total loss was not so great as in the other patients. The fact that this patient was in nitrogen balance after only two weeks does seem significant.

The level of nitrogen metabolism, 0.15 gm. per kg. per day, is not greatly depressed by rigid dieting of this type, even after periods of six to nine months. The average drop in absolute nitrogen

TABLE IV.—AVERAGE DAILY NITROGEN EXCHANGE. INCREASED CARBOHYDRATE PERIOD.

Case.	Days.	Weight.					Intake.					Nitrogen output.			Nitrogen balance, gm.	Nitrogen per kg. actual weight.	Nitrogen per kg. ideal weight.
		Initial, kg.	Ideal, kg.	Excess, per cent.	Average for period, kg.	Final, kg.	Calories.	Protein, gm.	Carbohydrate gm.	Fat, gm.	Nitrogen, gm.	Urine, gm.	Feces, gm.	Total, gm.			
1	200	148.0	61.2	141	125.1	105.5	586	59	41	20	9.4	8.7	0.6	9.3	0.1	0.078	0.16
2	8	104.0	65.9	58	103.6	103.2	525	65	50	7	10.3	9.7	1.0	10.7	−0.4	0.100	0.16
3	37	145.0	67.1	116	137.5	132.1	383	64	20	5	10.2	10.0	1.4	11.4	−1.2	0.083	0.17
4	139	178.6	70.9	151	161.5	147.3	371	65	16	5	10.4	8.6	1.0*	9.6	0.8	0.060	0.13
5	121	143.2	64.5	122	131.5	122.9	357	53	20	7	8.4	7.0	1.0*	8.0	0.4	0.060	0.12
Average	101	143.8	65.9	118	131.8	122.2	444	61	29	9	9.7	8.8	1.0	9.8	−0.1	0.072	0.15

* Estimated.

NOTE (Table IV).—The figures given in Table IV for the intake of patient No. 1 are the average values for the entire third period. The protein intake was approximately constant except for the twenty-second week, but several changes were made in the carbohydrate intake. Fifty grams of carbohydrate per day were given for the first three weeks after which the amount was reduced to 25 gm. In the nineteenth week the carbohydrate was increased to 90 gm. per day because of the depression in level of nitrogen metabolism and dissatisfaction with the monotonous diet. During weeks 22 and 23, it was further increased to 130–140 gm. per day, because of a plastic operation on her arms which took place on the fourth day of the twenty-second week. The operative wounds having healed well except for one small sinus, the carbohydrate was reduced to 25 gm. at the beginning of the twenty-fourth week. The last ten days of her stay were devoted to the working out of a discharge diet and the average carbohydrate intake amounted to 109 gm.

exchange is 10 per cent as compared with the preliminary period. In comparison to actual weight, the ratio of nitrogen to body weight becomes 0.072, due to the marked drop in the average weight. The nitrogen level, however, fluctuates greatly from week to week, the extremes being found in Patients 1, 4 and 5. Patient 1 showed minimum values of 0.12 in the first and nineteenth weeks and a maximum value of 0.20 in the twenty-fifth week. The lowest level in Patient 4, 0.11, occurs in the fourteenth week and the maximum, 0.16, in the eighteenth. Patient 5 reached the lowest level, 0.10, in the fourth, twelfth and sixteenth weeks and the highest, 0.15, in the seventeenth. The fluctuations in nitrogen level are not isolated "sports." An examination of the nitrogen curves shows a definite tendency toward maximum-minimum cycles of four to eight weeks' duration. The true significance of these cyclic variations is not apparent, but they appear to be unrelated to nitrogen intake or to variation in the rate of weight loss. The high level of nitrogen metabolism in Patient 1 during the last five weeks is not explained. The possible relationship of this phenomenon to aplastic operation in the thirty-second week is problematical.

Summary. 1. *Intake.* The protein intake of 5 obese patients on a freely selected diet which was almost adequate in calories corresponded to approximately 1 gm. per kg. of the ideal weight of these patients. During the second period, that of the reduction diet with low carbohydrate, the intake fell to 0.9 gm. due to the monotony of the diet, in spite of efforts to maintain the intake of 1 gm. per kg. By the addition of 20 gm. of carbohydrate to this reducing diet, a much more palatable menu was designed and less difficulty was experienced in maintaining a protein intake of slightly better than 0.9 gm. per kg. for period of six to nine months, although the calorific value of this diet remained below 450 calories per day. It is worthy of note that the diets employed were in no sense high protein diets, the protein content falling well below the new low normal figures of 80 gm. per day (Beard, Denis and Borgstrom). The term "maintenance protein diet" seems more appropriate.

2. *Output.*—The nitrogen output essentially paralleled the intake in the preliminary period of free choice. With the institution of a 350-calorie diet, there was a rise in output of 40 per cent which lasted for two or three days. The output then dropped rapidly, but remained slightly above the initial level throughout the second period (Table III). Upon the addition of 20 gm. of carbohydrate to the diet in the third period, the nitrogen output reached the initial level or fell below it. Although the actual daily output varied as much as 20 to 30 per cent from the average throughout the third period of seventeen to twenty-eight weeks, the average output for this entire period was only 10 per cent below the earlier periods.

3. *Balance.*—Balancing the intake and output of nitrogen for the three periods reveals certain important facts. Although the pre-

liminary period was too brief to permit nitrogen stabilization, these patients were essentially in balance at 11 gm. of nitrogen on a 2400-calorie diet.

At the outset of the second period a marked loss of body nitrogen occurred due to the increased output. The average loss was 2.0 gm. per patient per day, or 78 gm. per patient for the period. Since the 4 patients who were studied lost an average of 15.7 kg. of body weight in the thirty-nine days, this 78 gm. of total nitrogen lost for the same period indicates a small but appreciable loss of body nitrogen. That this loss is of little practical significance is suggested by a comparison with the nitrogen loss of the undernourished patients of Benedict as analyzed by Lusk.[5] Benedict's men lost 65 gm. of nitrogen and 4.5 kg. of weight in three weeks on a 1375-calorie diet. On the basis of Lusk's figure, 1 kg. of body weight contains 30 gm. of nitrogen, those subjects lost 2 kg. of protein tissue. Expressing these facts in another way, Lusk finds that they lost 3.2 per cent of the total body nitrogen, but 6.5 per cent of the total body weight.

TABLE V.—NITROGEN AND WEIGHT LOSS IN UNDERNOURISHED AND IN REDUCTION PATIENTS.

	Under-nourished.*	Period II.	Period III.
Duration, weeks	3	5½	14½
Diet, calories	1375.	336.	444.
Daily nitrogen output, gm.	11.3	11.4	9.8
Daily nitrogen loss, gm.	3.1	2.0	0.1
Total nitrogen loss, gm.	65.	78.	10.
Estimated initial body nitrogen content, gm.	2037.	1970.	1980.
Reduction body nitrogen, per cent	3.2	3.9	0.5
Initial body weight, kilo	67.9	159.2	143.8
Ideal body weight, kilo	....	65.6	65.9
Body weight loss, kilo	4.5	15.7	21.6
Weight loss (initial body weight), per cent	6.5	9.8	15.0
Weight loss (ideal body weight), per cent	....	24.0	32.0

* Lusk.[5]

In the development of a comparable statement for our patients, we have employed the ideal weight as indicative of the minimal total nitrogen content of the body. The 78-gm. nitrogen loss in five and a half weeks of this second period corresponds to less than 3.9 per cent of the total body nitrogen. Of equal significance, however, is the fact that this loss accompanied a loss of body weight equivalent to 10 per cent of the actual weight, but to 24 per cent of the ideal weight.

Throughout the third period it was observed that the patients were practically in nitrogen balance, as shown by the average figures. At this time, however, a new phenomenon appeared in the form of successive periods of loss and gain of nitrogen, but such that at the

end of six to eight week cycles there was no appreciable alteration of the total nitrogen content of the body. The full significance of this phenomenon is not apparent, although it is conceivably related to the well-known temporary protein storage mechanisms. A comparison of the figures for the whole one hundred and one days of this third period of reducing diet with increased carbohydrate with those of Benedict, as above, shows even more striking results (Table V). Our patients, on diets of approximately one-third of the caloric value of Benedict's, lost but 10 gm. of nitrogen in fourteen and a half weeks. This loss is 0.5 per cent of the estimated total body nitrogen, and is to be contrasted with the 21.6 kg. of total weight loss or its equivalents, 15 per cent of the actual weight and 32 per cent of the ideal weight. Such ratios suggest that relatively little body protein was lost by our patients in the third period.

The fluctuations in nitrogen balance which have been observed in the successive dietary periods may be in part explained as dependent upon two factors. With the abrupt institution of the low carbohydrate diet at the outset of Period 2, an appreciable amount of protein was required for its antiketogenic properties. Upon the adaptation of the body to its new energy supplies, this factor diminished rapidly. Subsequently, the maintenance of balance appears to depend upon the ingestion of adequate nitrogen (Period 3). The increase of carbohydrate in the diet from a ratio of 1 gm. to each 6 of protein to 1 gm. for each 2 of protein permits the development of a more palatable menu and, therefore, the desired protein intake while increasing the caloric value only 100 calories.

4. *Level.* The level of nitrogen exchange at which these patients operated at the onset, 0.16 gm. of nitrogen per kg. of ideal weight, does not differ significantly from the figures of Beard and Denis and Borgstrom for normal persons. With the institution of the 350-calorie reduction régime, a 30 to 40 per cent increase in nitrogen metabolism occurred which was followed in most cases by a rapid return to normal (Table III). The suggestion is offered that this phase represents a period of readjustment of the body to its major sources of energy supply, during which much protein was utilized for its antiketogenic properties. Following this readjustment, the organism appears to function at approximately the initial level of 0.16 gm. of nitrogen per kg. of ideal body weight. In view of the marked loss of weight which took place during this 350-calorie diet period, this observation indicates the absence of physiological starvation with its concomitant depression of nitrogen metabolism. The numerous investigations of starvation which are described at length by Lusk[6] show characteristically prompt depressions of nitrogen level amounting to 30 per cent or more in short experiments and to 50 and 80 per cent in those running from three to four weeks. The increase in the diet of our patients to 450 calories by the addi-

tion of 20 gm. of carbohydrate had little influence upon the level of nitrogen exchange. Two patients, Nos. 4 and 5, did reduce their metabolic level, giving averages of 0.13 and 0.12 respectively for the third period. The average of all patients, however, is reduced to only 0.15, which is but slightly below the levels of the first and second periods.

In the comparison of the average levels of nitrogen metabolism for such a short series, reservations must, of course, be made for the unweighted influence of certain variant data upon the average figures. Patients 2 and 3, for example, were omitted from Periods 1 and 2 respectively, which prevents direct comparison of the weight averages. The high nitrogen level of Patient 4 in Period 1 and of Patient 2 in the second period tend to elevate the average values of these periods. In the latter case this single high figure is to a large extent responsible for the apparent increase in output for the period. In addition to these examples we have to consider in the third period the high level of Patient 3 which influences the average unduly. It may be recalled, furthermore, that the two-week period of nitrogen readjustment and loss took place in this case in the third period in contrast to all other cases. Finally, the inclusion of the short-term patients, No. 3, and more especially No. 2, elevates artificially a properly weighted average for the nitrogen level of Period 3. In view of the fact that the average of the nitrogen levels of only the 3 long-term patients is 0.14 as contrasted to 0.15 for the entire group, it would appear that the use of unweighted averages produces errors of degree rather than of direction of change. In general, it seems that a dietary régime of this type can be continued for six to nine months without a serious depression of nitrogen exchange below the initial level.

Conclusions. 1. The level of nitrogen metabolism in obese patients does not differ from that of normal persons.

2. The rapid reduction of weight of these patients by a "maintenance protein diet" produces only a slight depression in nitrogen level even after seventeen to twenty-eight weeks.

3. During the early weeks of rigid dieting patients lose body nitrogen to the extent of 3 to 6 gm. per day before the reëstablishment of nitrogen equilibrium.

4. The total loss of nitrogen in the period of negative balance amounts to less than 4 per cent of the total body nitrogen.

5. The early loss of nitrogen is associated with a marked rise in nitrogen output, possibly due to the use of protein for its antiketogenic properties.

6. Obese patients may be maintained in nitrogen balance at normal levels, but in negative carbon balance on diets containing 350 to 450 calories, provided that the protein intake of 1 gm. per kg. of ideal weight can be maintained.

7. The maintenance of protein intake can be more readily secured by feeding diets containing $\frac{1}{3}$ to $\frac{1}{2}$ gm. of carbohydrate for each gram of protein than by lower ratios.

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CREATININ EXCRETION IN ABNORMAL STATES OF NUTRITION.

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The generally accepted conception of the metabolism of creatinin holds that urinary creatinin is a product of muscle metabolism and is an index of muscle mass and efficiency. This paper reports observations on the creatinin excretion of 5 obese patients and 5 patients of subnormal weight during dietary correction with special reference to possible alterations in their muscle mass. Four normal individuals are included as controls.

The investigations of creatinin metabolism which led to the development of the current theories were inaugurated by the introduction of the colorimetric method of analysis of Folin in 1904.[1] Shortly thereafter Folin[2] showed that the excretion of creatinin on a meat-free diet was constant for the individual and totally independent of the other elements of nitrogen metabolism. This work has been repeatedly confirmed. Variations among individuals are dependent largely, but not wholly, on variations in body weight. To demonstrate this relationship, Folin[1] calculated the number of milligrams of creatinin eliminated per kilogram of body weight. Shaffer[3] called this expression the "creatinin coefficient" and substituted, in the expression, the number of milligrams of creatinin

nitrogen for the number of milligrams of creatinin. It is in these terms that it is now usually expressed.

The creatinin excretion is influenced by diet, but for the purpose of this study this is not an important factor. The amount of creatinin, *per se*, found in foodstuffs is negligible. Benedict and Osterberg[4] and Chanutin[5] have proven the conversion of creatin into creatinin and the direct influence of creatin ingestion on creatinin excretion. Creatin is found in meats in quantities varying from 0.2 per cent to 0.5 per cent but is negligible in other foodstuffs. Ringer and Raiziss[6] demonstrated that a low-protein, meat-free diet over a period of several months would result in a gradual and steady decline in creatinin excretion not dependent upon variations in body weight. Starvation experiments have consistently shown a progressive lowering of creatinin output at a rapid rate.[7]

Other factors influencing the excretion of creatinin are age, sex and muscle mass and efficiency. Repeated observations[8] have shown the creatinin excretion to be at a low level during the early weeks of life and to increase to reach a constant level at about the time of puberty. In general, the excretion of women is lower than that of men. The average of the coefficients found by a group of investigators[8] was nine for men and six for women. This lower figure in women was considered by Shaffer to be not an effect of sex itself but rather of a greater proportion of adipose tissue and of a lower muscular development. This view is supported by the work of Tracy and Clark[9] and of Hodgson and Lewis[10] showing that the creatinin coefficients of women trained in physical education correspond to those of men.

Myers and Fine[11] and Palladin[12] have shown a direct relationship between the creatinin coefficient and the total body creatin in the individual and in the species. Since muscle creatin comprises fully 98 per cent of the total body creatin[13] urinary creatinin becomes, for practical purposes, an index of muscle creatin or of muscle mass and the creatinin coefficient an index of muscle mass as related to body weight.

The studies here reported were made on patients who were under observation on the metabolic pavilion of the hospital for periods varying from sixteen to one hundred and thirty-three days. Four of 5 obese patients studied were normal except for their excess weight. The fifth patient in this group exhibited a mild, uncomplicated diabetes, readily controlled by diet. All were being reduced by the method described by Strang, McClugage and Evans.[14]

The underweight patients were cases of: (1) Pyelitis; (2) subacute bacterial endocarditis; (3) chronic malnutrition; (4) chronic malnutrition, and (5) convalescent lobar pneumonia and empyema. This last patient represented, from a metabolic point of view, a starvation patient. During the period of observation they were on balanced general diets of high caloric values. No restrictions were placed upon their dietary.

The group classed as "normal" were all within 10 kilos of the theoretical ideal weight. One individual within 4 kilos of the ideal weight was placed on a balanced maintenance diet. Two less than 10 kilos in excess of the ideal weight were on the reduction diet. The other patient less than 10 kilos below the ideal weight received a balanced high caloric diet.

The creatin content of the diets given was calculated as 0.5 per cent of the meat given. On this basis (a liberal estimate), the creatin intake did not in any case exceed 1.2 gm. per day, and it was practically a constant factor.

Twenty-four-hour urine specimens were collected and preserved with toluene on ice. During the early period of the observation samples of the mixed specimen of the week were analyzed. Later, a sample of a single days' collection was analyzed and the figure used as the average for the week. There was no variation in the results obtained by the two methods. Creatinin determinations were made by the method of Folin.[15] The picric acid used was within the limits of purity specified by Folin and Doisy.[16] All urine specimens were negative for acetone and diacetic acid.

In one of the obese patients, 4 of 6 observations yielded creatinin nitrogen figures between 0.51 and 0.55 gm. per day. Two observations yielded outputs of 0.18 and 0.29 gm. per day. The nitrogen excretion, weight change and other observations taken at the same time showed no such variation.[17] We are unable to explain the discrepancy. In all other cases the figures for the average daily creatinin nitrogen did not vary from week to week more than 0.19 gm.

TABLE I.

	Creatinin nitrogen excretion, gm. daily.	Observed weight, kg.
Obese	0.42	137.0
Normal	0.49	64.6
Variation	0.07	72.4

The average daily excretion of creatinin nitrogen of the 5 obese patients was practically the same as that of the 4 normal individuals. (Table I.) The average of the creatinin coefficients calculated from these figures on the basis of the observed weights was lower than that of the normal individuals. The variation from the normals was in inverse proportion to the degree of obesity. When, however, the creatinin coefficient was calculated on the basis of the ideal weight it was within normal range. (Table II.) During the reduction of the obese patients by dietary measures alone, the creatinin excretion did not decrease in proportion to the loss of weight or, which we feel is an important observation, in a manner comparable to that seen in starvation, as shown by Benedict and Cathcart.[7] There was no exception to this observation, even in one patient reduced 36 kg. in body weight.(Table III.)

TABLE II.

	Obese.	Normal.
Average theoretical ideal weight (kg.)	65.4	62.2
Average observed weight (kg.)	137.0	64.6
Average creatinin coefficient ideal weight	6.7	7.9
Average creatinin coefficient observed weight	3.4	7.7

TABLE III.*

Period of observation, weeks.	Creatinin N. excretion, daily.	Creatinin N. excretion, Cathcart, 1907.	Creatinin N. excretion, Benedict, 1915.
First	0.39	0.45	0.50
Second	0.52	0.38	0.48
Third	0.42	....	0.38
Fourth	0.46	....	0.34
Fifth	0.46	....	0.33
Sixth	0.48		
Seventh	0.47		
Eighth	0.43		
Ninth	0.39		
Tenth	0.35		
Eleventh	0.37		
Twelfth	0.46		
Thirteenth	0.35		
Fourteenth	0.44		
Fifteenth	0.44		
Sixteenth	0.44		
Seventeenth	0.40		
Eighteenth	0.44		
Nineteenth	0.44		

* The figures in this table are those of a patient reduced 36 kg., and are typical of the entire group. The figures of Cathcart and of Benedict are converted to weekly averages for purposes of comparison.

The average daily excretion of creatinin nitrogen in the 5 patients of subnormal weight was decidedly lower than that of the normal individuals. (See Table IV.) The creatinin coefficients of these patients calculated on the basis of their observed weights was at the lower limit of the normal range. Calculated on the basis of their ideal weights it was below the normal in direct proportion to the degree of undernutrition. (See Table V.)

TABLE IV.

	Creatinin N. excretion, gm. daily.	Observed weight, kg.
Underweight	0.28	47.5
Normal	0.49	64.6
Variation	0.21	17.0

TABLE V.

	Underweight.	Normal.
Average theoretical ideal weight (kg.)	63.4	62.2
Average observed weight (kg.)	47.6	64.6
Average creatinin coefficient ideal weight	4.4	7.9
Average creatinin coefficient observed weight	5.8	7.7

The patient mentioned above as being considered a starvation patient showed an extremely low excretion of creatinin nitrogen and a low coefficient with a rapid return toward normal, paralleling weight gain. (See Table VI.)

TABLE VI.

Period of observation, weeks.	Creatinin N. excretion, gm. daily.	Observed weight, kg.
First	0.18	46.6
Second	0.21	49.8
Third	0.25	52.5
Fourth	0.37	55.3
Fifth	0.37	58.2

The independence of creatinin excretion from the other elements of nitrogen metabolism, which has been reported by others, was observed in these studies. There was no relation between the creatinin excretion and the total urine volume and it was independent of the total nitrogen excretion and presence of positive or negative nitrogen balance.

Our findings are in accord with those of previous investigators relative to the practical but not absolute constancy of creatinin excretion in the individual. The variation from the mean daily excretion did not exceed 0.12 gm. in any case. They are also in accord with the results reported in the literature of creatinin excretion in the obese. Clinically our series conforms to the descriptions previously recorded as regards the correlation of muscular development and creatinin excretion. Without exception our patients exhibiting a high creatinin coefficient were well-muscled individuals whereas those exhibiting a low coefficient, as figured on their actual but not ideal weight, were either poorly muscled or excessively obese.

Assuming as valid the direct relationship between creatinin excretion and muscle mass, our results support the hypothesis that the excess weight of the obese is due to increase in adipose tissue. The fact that they exhibit a normal coefficient when calculated on the basis of the ideal weight indicates an essentially normal muscle mass. Our results also support the contention that reduction by dietary measures occurs chiefly at the expense of fat. As evidenced by the actual creatinin nitrogen excretion, the muscle mass of our patients was unchanged even after the reduction of as much as 79 pounds of body weight. The average creatinin nitrogen excretion of the obese group was exactly the same for the last week of the period of observation as for the first week, in spite of an average reduction of 21.2 kilos in weight. (See Table VII.) In each case during the latter half of the period of observation the excretion averaged from 0.02 to 0.03 gm. lower than during the first half. This change is within the limits of error of the method and is not significant.

TABLE VII.

Patient.	First week. Creatinin N., gm. daily.	First week. Average weight, kg.	Last week. Creatinin N., gm. daily.	Last week. Average weight, kg.
B. J.	0.39	170.3	0.44	134.3
M. F.	0.39	113.1	0.49	103.6
E. M.	0.46	144.3	0.34	122.8
M. R.	0.39	179.2	0.39	152.4
I. F.	0.55	145.5	0.51	133.4
Average	0.43	150.5	0.43	129.3

Our patients of subnormal weight showed creatinin coefficients slightly below the normal individuals. This is not in accord with the observations of McLaughlin and Blunt[18] on women, or of Wang, and others[19] and Rougichitch[20] on children of subnormal weight. These investigators found, in such cases, higher coefficients than in corresponding normal individuals. Hunter in referring to their work suggests that their findings may indicate the effect of a fat deficiency. The low coefficients in our series would indicate that these individuals are deficient in muscle mass as well as in adipose tissue. During their period of gain in weight, however, they did not show a significant increase in creatinin excretion. The average excretion for the last week was, in fact, 0.03 gm. lower than for the first week. (See Table VIII.) In each case the excretion during the last half of the period differed from that of the first half by −0.01 gm. to −0.05 gm. creatinin nitrogen daily. These changes are not significant.

TABLE VIII.

Patient.	First week. Creatinin N., gm. daily.	First week. Average weight, kg.	Last week. Creatinin N., gm. daily.	Last week. Average weight, kg.
K. McD.	0.31	45.1	0.29	48.4
K. A.	0.34	41.7	0.26	52.7
L. P.	0.27	47.4	0.24	58.7
F. M.	0.19	34.9	0.20	42.5
Average	0.28	42.3	0.25	50.4

The case reported in Table VI, that of a man convalescent from a protracted course of lobar pneumonia and empyema, who at the onset of the observations was extremely emaciated and for our purposes a starvation patient, differs from the other 4. The strikingly low creatinin excretion at the onset with rapid rise reaching a plateau before his gain in body weight had ceased suggests the attainment of the level of creatin saturation in the muscles and also a rapid gain in body musculature. This finding indicates that there may be a fundamental difference between acute starvation and chronic malnutrition.

The group of "normals" showed no important change in either weight or creatinin excretion. Creatinin nitrogen excretion for the last week averaged 0.03 gm. more than for the first week with an average loss of 1.6 kilos in weight. (See Table IX.) During the latter half of the period of observation the creatinin nitrogen excretion in each case, varied from −0.01 to +0.04 gm. as compared to the first half period.

TABLE IX.

Patient.	First week. Creatinin N., gm. daily.	First week. Average weight, kg.	Last week. Creatinin N., gm. daily.	Last week. Average weight, kg.
H. B. M.	0.54	75.4	0.47	66.5
S. M.	0.48	66.6	0.47	64.3
R. C.	0.51	59.9	0.70	60.2
M. B.	0.44	62.2	0.44	62.5
Average	0.49	66.0	0.52	64.4

Conclusions. 1. The creatinin excretion of obese patients corresponds very closely to that of normal individuals. When reduced by dietary measures alone, the amount of creatinin excreted does not change appreciably. If the coefficient of creatinin excretion is an index of muscle mass, this indicates that the excess weight of the obese is due to adipose tissue alone and that when reduced by the dietary methods here employed, the reduction is not at the expense of muscle tissue.

2. The creatinin excretion of patients of subnormal weight is markedly reduced as compared to the normal. This indicates that in malnutrition the muscle mass as well as adipose tissue is diminished.

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THE SIMULTANEOUS OCCURRENCE OF PEPTIC ULCER AND DIABETES OR GLYCOSURIA.

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We are reporting a group of 11 cases in which a peptic ulcer was present simultaneously with diabetes mellitus or glycosuria. We do so for the following reasons: (1) Because many ulcers are overlooked in the presence of diabetes; (2) because a peptic ulcer may cause glycosuria; (3) because the presence of the two diseases complicates the management of the patient and may lead to unfortunate results; (4) because diabetes may simulate ulcer pain even in the absence of an ulcer; (5) because a diabetic diet may activate a dormant ulcer.

Peptic ulcer and diabetes mellitus are common diseases of adult life. Each disease may be present without definite symptoms or knowledge of its presence by the sufferer. Suffice it to mention the frequency with which diabetes mellitus is first recognized in the course of a health or life-insurance examination. The first manifestation of an ulcer may be a complication, like perforation or hemorrhage. It is interesting to note that Joslin,[1] first recognized peptic ulcer in diabetes in 1923 in a case of perforation and since has demonstrated the condition in an increasing number of cases, totaling 19 patients with duodenal and 9 patients with gastric ulcer. On checking up his past cases he found that in the first 2700 of diabetes mellitus no ulcer was recognized. Calvert,[2] reports 7 cases, Fitz,[3] 1 case, and Holcomb,[4] 1 case. We have observed 6 cases.

Peptic ulcers may cause glycosuria through a pancreatitis either by direct contact where the base of the ulcer is adherent to the pancreas or by a secondary low-grade infection of the adjacent organs, such as the liver and pancreas. This is particularly true of penetrating lesions of the posterior wall of the stomach. Evidence of the interrelation is afforded by the results of treatment, where the glycosuria disappears on ulcer régime without restriction of carbohydrates. Van der Bergh,[5] reports 8 such cases, Meyer,[6] 2 cases; we have observed 3 such cases.

Both diabetes and ulcer are diseases amenable to dietetic care. Their management requires careful coöperation on the part of the patient, but also intelligent guidance by the physician for the dietetic problem is a more difficult one.

The hunger in untreated diabetes may at times mask the hunger pain of an ulcer. In this way ulcers are probably overlooked. Hypoglycemia following insulin may likewise cause hunger pain. In all types of hunger distress the pain is relieved by food. The findings on examining the gastric contents are not diagnostic, for severe diabetes mellitus is frequently associated with low acidity; hypoglycemic states with hyperacidity.

The diet usually prescribed to patients with diabetes contains a considerable amount of roughage and is therefore unsuitable in treating cases of peptic ulcer. It may even activate a dormant ulcer, aggravate the symptoms or cause a gastric or duodenal hemorrhage or perforation. The ulcer diet, on the other hand, is suitable for the treatment of mild or moderate diabetes. Some simple individual modifications may at times be necessary in the convalescent Sippy diet to keep the patient sugar free. If the diabetes is not controlled on this régime, insulin should be used. In none of our cases, however, was insulin necessary, for in all of them the diabetes was mild. We have never observed an ulcer in severe diabetes. Whether this is because of the low acidity found in severe diabetes, we cannot state.

Eleven cases of peptic ulcer with glycosuria observed by us have been classified as follows:

1. Diabetes complicated by peptic ulcers.
2. Peptic ulcers complicated by glycosuria.
3. Ulcers and glycosuria, interrelationship uncertain.

Diabetes Complicated by Peptic Ulcers. We saw 6 cases of true diabetes mellitus and peptic ulcer. The diabetes was mild in all these cases and was controlled by diet without insulin. Digestive symptoms persisted in all of them until an ulcer régime was instituted. One case (G. C.) did not improve on medical ulcer régime and surgery is considered. It is interesting to note that all these ulcers were duodenal.

Case Reports. Case I.—F. M. G., male, aged fifty-four years, tailor, seen in 1927, had diabetes mellitus for four years, which was controlled by a proper diet. In 1926 he developed epigastric pain, which was worse on exercise of one-half to one hour after meals. He did not take alkalis habitually. A Roentgen ray examination six months after the onset of the digestive symptoms showed a duodenal ulcer. Four months later the ulcer perforated. At operation the perforation was closed without excision of the ulcer or gastroenterostomy. Patient since has had no symptoms related to ulcer and his diabetes is under control on a modified ulcer diet without insulin. Diagnosis: Diabetes mellitus, duodenal ulcer with perforation.

Case II.—G. C., aged thirty-six years, single, grocer, seen in 1929 (Beth Israel Hospital No. 508), had a diagnosis of mild case of diabetes mellitus in 1917 and since then the urine has been sugar free most of the time on a

slightly restricted diet. In 1928 he developed epigastric pain, also heartburn and belching coming two or three hours after meals. Patient likewise complained of night pain. The pain was relieved by soda bicarbonate or food. A Roentgen ray examination showed a duodenal ulcer with 20% six-hour gastric residue. Two sugar-tolerance tests were performed. The urines were positive on testing for sugar and the blood-sugar curves were characteristic of diabetes mellitus. The diabetes was controlled by a modified ulcer diet without insulin, but the ulcer pain persisted. He was therefore advised to undergo operation for his ulcer, but refused. Diagnosis: Diabetes mellitus, duodenal ulcer with mild gastric stasis.

CASE III.—G. S., aged sixty-five years, male, railroad laborer (Beth Israel Hospital No. 9073 A), was admitted in 1929 to this hospital because of hematemesis five days previously. During the preceding six weeks patient complained of gas pain, coming two hours after meals. A routine urine examination disclosed glycosuria. Blood-sugar examination four hours after a meal showed hyperglycemia. At a later Roentgen ray examination a duodenal ulcer without pyloric obstruction was found. Patient became symptom free on a modified ulcer diet. The diabetes was controlled by this diet without the administration of insulin. Diagnosis: Diabetes mellitus, duodenal ulcer.

CASE IV.—I. L., aged fifty-eight years, male, carpenter (Beth Israel Hospital No. 4056 A), was first referred to the diabetic clinic in 1929 for diabetes mellitus which was discovered on admission to the outpatient department. The urine showed a reddish-brown precipitation on testing for sugar. There was a definite hyperglycemia. Intermittent substernal pain had been present one and a half years. He also had frequent attacks of hypochrondrial and umbilical pain. There was no food relationship to the pain. On a diabetic diet without insulin the glycosuria disappeared and the blood sugar returned to normal. The digestive symptoms, however, became aggravated. Roentgen ray examination revealed a duodenal ulcer. The patient therefore was given a modified ulcer diet and his digestive symptoms disappeared without the reappearance of glycosuria. Diagnosis: Diabetes mellitus, duodenal ulcer, hypertension, angina pectoris.

CASE V.—I. W., aged sixty-eight years, female, housewife (Beth Israel Hospital No. 2752 A), had a diagnosis of diabetes mellitus made in 1925. The diabetes was under control by diet without insulin. She was seen by us in 1929, complaining of epigastric pain, of two months' duration. This pain was related to food, coming on one to two hours after meals. There was a history suggestive of tarry stools. She lost considerable weight. A barium-series examination showed a duodenal ulcer without pyloric obstruction. She was given a modified ulcer diet. This was followed by improvement of her digestive symptoms and a gain in weight. No insulin was required. Diagnosis: Diabetes mellitus, duodenal ulcer.

CASE VI.—L. G., aged fifty-eight years, male, tailor (Beth Israel Hospital No. 1953), was referred to the diabetic clinic of the outpatient department in 1929 with the diagnosis of diabetes mellitus of three years' duration. The diabetes was under control on a liberal diabetic diet rich in roughage without insulin. A barium-series examination revealed a duodenal ulcer without obstruction. On an ulcer diet patient became symptom free without reappearance of glycosuria. Unfortunately, he developed uremia and died. Diagnosis: Diabetes mellitus, duodenal ulcer, chronic nephritis, uremia.

Peptic Ulcers Complicated by Glycosuria.

CASE VII.—S. A., male, aged forty-five years, junk dealer (Old Beth Israel Hospital No. 6408), was admitted to the hospital in 1926 with a history of heartburn, distention, and epigastric pain related to meals of six months' duration. He also had night pain. There was no distinct relief by food and soda. Repeated urine examination showed traces of sugar. Fasting blood-sugar test showed no hyperglycemia. Barium-series examination revealed a large posterior wall penetrating gastric ulcer. On a Sippy diet the digestive symptoms disappeared and repeated urine examinations showed no sugar. Patient died three years later from coronary thrombosis. Diagnosis: Gastric ulcer, temporary glycosuria, ? chronic pancreatitis.

CASE VIII.—S. N., male, aged fifty-six years, tailor, since 1916 complained of indefinite epigastric distress at irregular intervals. Since 1925 discomfort has been almost continuous. He also had attacks of pain in the right upper quadrant. He was seen in 1926 in one of these attacks when marked tenderness was found over the gall-bladder region. The urine contained a large trace of sugar. Chronic cholecystitis with an acute pancreatitis was suspected. At the operation a chronic pyloric ulcer the base of which was formed by the pancreas was found. No gall-bladder pathology was found. A gastroenterostomy was performed. Since then the patient has been symptom free and the urine has been sugar free on several examinations. Diagnosis: Pyloric ulcer, chronic pancreatitis.

CASE IX.—M. S., male, aged fifty-two years, shoemaker (Old Beth Israel Hospital No. 3072 and 4412), was seen in 1925 for digestive symptoms of twelve years' duration. He had intermittent hunger pain in the epigastrium, relieved by food and soda. He had frequent attacks of vomiting, bringing up at times very large quantities. On two occasions he had severe hematemesis. Two years before admission a resection of adhesions about the stomach and duodenum had been done. The urine examination on various occasions showed a small to a large trace of sugar. A barium-series examination showed a duodenal ulcer with 60% six-hour gastric stasis. At operation a large duodenal ulcer, the base of which was the head of the pancreas was found. There were numerous adhesions. A gastroenterostomy was performed and followed by a six months' ulcer régime. He remained symptom free and his urine was sugar free on several examinations. Diagnosis: Duodenal ulcer with obstruction, chronic pancreatitis.

Ulcers and Glycosuria-interrelationship Uncertain. The third group consists of 2 cases. They showed an ulcer and glycosuria, but one cannot be certain whether the glycosuria is caused by the ulcer or whether it is a true diabetic glycosuria.

CASE X.—E. K., female, aged fifty-eight years (Beth Israel Hospital No. 7648 A), was referred to the diabetic clinic because of frequent glycosuria. She showed slight hyperglycemia one and a half hours after a meal containing about 50 gm. of carbohydrates. She complained of indefinite digestive symptoms of three years' duration, and had been troubled by a few attacks of right upper quadrant pain, requiring morphia. Two Roentgen ray examinations of the digestive tract in two different hospitals were negative. After a diabetic diet had been given for three months the urine continued to show occasional traces of sugar. The digestive symptoms gradually became more severe, therefore, a third Roentgen ray examination was made and revealed a duodenal ulcer. Patient was therefore given a modified

ulcer diet. The digestive symptoms improved during the next two months. The urine became sugar free most of the time. Diagnosis: Duodenal ulcer, ? cholecystitis, ? diabetes.

CASE XI.—Z. L., male, aged seventy-seven years, watchmaker (Beth Israel Hospital No. 1497 A), was seen in 1929 complaining of digestive symptoms of four years' duration, consisting of heartburn, belching, and epigastric pain related to meals. Repeated urine examinations showed a glycosuria of varying degrees. A glucose-tolerance test with 50 gm. glucose showed a moderate hyperglycemia and a delayed blood-sugar curve with a slight glycosuria. A barium-series examination revealed a duodenal ulcer. Patient was given a modified ulcer diet with almost complete relief of digestive symptoms. The urine on repeated examinations was sugar free. Diagnosis: Duodenal ulcer, ? diabetes mellitus.

Discussion. A group of 11 cases of glycosuria with peptic ulcer have been presented. The diagnosis of ulcer was confirmed by Roentgen ray evidence in 10 cases, in the eleventh the diagnosis was made at operation; in many examinations of the gastric contents showed hyperacidity. Unfortunately a few did not have this examination. There were 2 cases with hemorrhage and 1 gave a history suggestive of bleeding. In 3 cases the diagnosis was confirmed at operation. One case is expected to undergo surgery for an ulcer not amenable to medical care. Two cases had partial pyloric obstruction. In 9 cases the ulcer was in the duodenum, in 2 in the stomach. Diabetes was definitely diagnosed in 6 cases. The diagnosis was confirmed by frequent blood-sugar tests and urinalysis, in 1 by a typical diabetic sugar-tolerance curve. Five cases had glycosuria and an ulcer. We believe 3 of these are caused by the ulcer, because the ulcer penetrated into the pancreas, proven at operation in 2 cases, in all 3 cases glycosuria disappeared with the healing of the ulcer. Two cases (X and XI) showed an impaired sugar-tolerance test and a definite duodenal ulcer. We are not certain, however, whether the ulcer is the cause of the glycosuria, or whether the glycosuria is a true diabetic one.

Diagnostic Difficulties. The group divides itself into two classes: (1) true diabetes mellitus and (2) glycosuria. The case with a large amount of sugar in the urine is at once classified as diabetic and the digestive symptoms are often interpreted as due entirely to the diabetes. However, two or more diseases may present themselves in the same patient. Digestive symptoms persistent after the diabetes is under control suggest pathology in the gastrointestinal tract. Hunger pain may be a confusing symptom in these cases, since it is present in ulcer, in uncontrolled diabetes, as well as in hypoglycemic states. Hypoglycemia can easily be ruled out by a blood-sugar estimation. A timely diagnosis is important because of the possible damage by a diabetic diet containing large amounts of vegetables. A definite diagnosis of peptic ulcer in diabetes can be made only on the basis of history, Roentgen ray evidence and therapeutic test.

In peptic ulcer with intermittent glycosuria, the latter is frequently overlooked because routine urinalysis is done only at long intervals. If glycosuria is discovered the question arises whether it is a true diabetic glycosuria or not. In these cases a sugar-tolerance test must be interpreted very carefully. Van der Bergh,[5] in a group of ulcers with glycosuria showed a curve, thought by him to be typical of ulcer cases. The curve is steep, but recedes to normal within two hours. However, he found some ulcer cases with glycosuria and a normal sugar-tolerance test.

We have repeated his sugar-tolerance test with 50 gm. glucose in a few ulcer cases without glycosuria and found a normal curve in all. In our cases of ulcers with glycosuria, we had occasion only twice to do a 50-gm. sugar-tolerance test and in both cases (X and XI) the curves were suggestive of diabetes. The curve of Van der Bergh is probably diagnostic of a low-grade pancreatitis of any cause. We feel that uncomplicated peptic ulcers have no impaired sugar tolerance. Glycosuria with an ulcer may be produced by a pancreatitis of any cause. If the glycosuria disappears under an ulcer régime we should feel justified in assuming that the pancreatitis is caused by the ulcer. Should the glycosuria persist after the ulcer became quiescent, other pathology causing pancreatitis should be considered. If such cannot be found, the case must be considered as a mild diabetic.

Treatment. The treatment is less difficult than it seems on first thought. In mild diabetes the ulcer diet is sufficient to control the glycosuria. The first stage Sippy diet, f.i., consists of 1000 gm. milk and 1000 gm. 20% cream daily, which gives CbH. 70 gm.; fats, 187 gm.; protein, 47 gm.; total calories, 2150. The only necessary modification is in the restriction of the amount of cream. The diet is gradually built up according to the Sippy régime bearing in mind the prevention of glycosuria and hyperglycemia. Should any difficulties in the control of glycosuria or hyperglycemia present themselves, insulin may be used. This is particularly true in the underweight patient. Some cases will need insulin only for a limited period. In pyloric obstruction insulin should be administered with the utmost care, as a hypoglycemia may occur, with retention of food in the stomach. Peptic ulcer with a nondiabetic glycosuria caused by an adjacent pancreatitis should be regarded more seriously. These cases do not always respond to the medical ulcer régime and surgical intervention is often necessary. In our cases 2 out of 3 were operated upon, Meyer's 2 cases had surgery.

Conclusions. 1. Peptic ulcer is frequently overlooked in cases of diabetes mellitus. With persistent digestive disturbances, particularly hunger pain, peptic ulcer should be suspected and carefully investigated.

2. The diabetic diet rich in roughage may activate a peptic ulcer.

3. Insulin when necessary should be used with great care in cases with pyloric obstruction.

4. A nondiabetic glycosuria in a case of peptic ulcer is suggestive of an adjacent chronic pancreatitis.

5. Surgery is indicated in the treatment of a peptic ulcer complicated by chronic pancreatitis.

Addendum. Since this paper has been written we have seen 2 more cases which belong to this group, namely; (1), posterior wall gastric ulcer with glycosuria; (2), a true diabetes with a definite duodenal ulcer by Roentgen rays.

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PROBLEMS OF CARDIAC DISEASE ASSOCIATED WITH URINARY RETENTION.*

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In recent years, urologists have recognized the importance of cardiac problems in cases of benign prostatic hypertrophy causing urinary obstruction. This has been fundamental in reducing the operative mortality, for practically all of these cases occur at a time of life when one most frequently recognizes diminished cardiac reserve secondary to arteriosclerosis, hypertension and other factors. In statistics recorded by Willius,[1] cardiovascular disease was demonstrated by electrocardiographic tracings in 42% of 705 cases with prostatic hypertrophy.

Since this association is so vital from a urological standpoint, it seems logical to ask, "What consideration is given by internists to factors essentially urological in male patients past middle life who show evidence of cardiac disease?" In the medical approach to a case presenting a predominantly cardiac picture, bladder obstruction is not usually searched for unless the symptoms and signs are outstanding. A urological history is rarely developed in as great detail as the cardiac history. Frequency and nocturia are too often dismissed as mere manifestations of passive congestion.

* Read before the Philadelphia Urological Society, February 24, 1930.

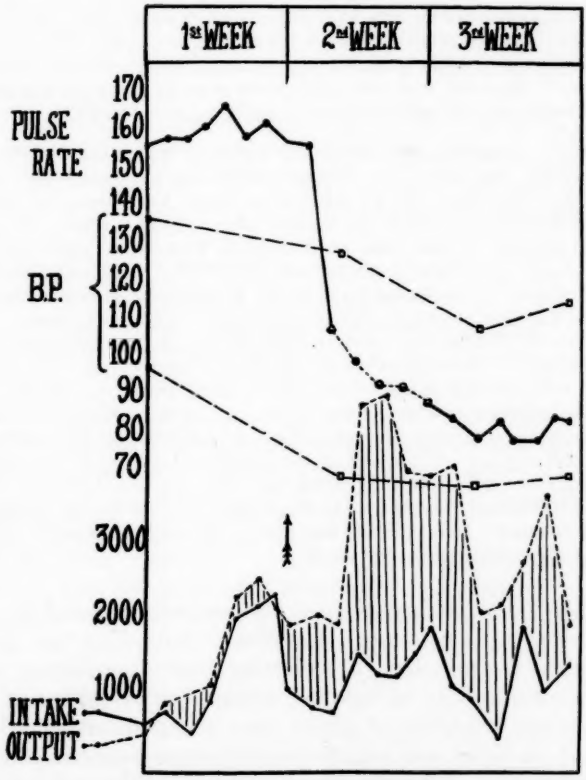
Residual urine estimations are seldom included in the medical work-up of a cardiac case. In brief, the importance of always recognizing even minor grades of bladder retention in the presence of myocardial insufficiency is not generally appreciated.

It is the purpose of this paper to discuss, from a medical viewpoint, the relationship between chronic bladder obstruction and cardiac disease, and to review the results obtained from bladder drainage in a group of 40 cases.

The following 2 cases are presented to show the effect which unrecognized mechanical factors in the lower urinary tract may exert on the cardiovascular system.

Case Reports. CASE I.—F. S., a man, aged fifty-two years, was admitted to the University Hospital, service of Dr. Stengel, with signs of advanced cardiac failure. For two years there had been increasing palpitation, dizziness, and precordial pain. For six months auricular flutter had

CHART I.



been recognized, and for two months previous to admission, dyspnea, edema, cough, and weakness became increasingly severe. Except for moderate frequency and nocturia, there were no symptoms referable to the urinary tract. Twelve years ago the patient had "inflammatory rheumatism."

The outstanding physical findings follow: Orthopnea, cyanosis, drowsiness, anasarca, pulmonary edema, cardiac enlargement to the left with a ventricular rate of 160, loud systolic murmur at the apex transmitted slightly into the axilla, blood pressure: 140 systolic, 98 diastolic, moderate arteriosclerosis, enlarged liver, and ascites. The electrocardiogram showed severe myocardial disease and auricular flutter.

The patient had been well digitalized previous to admission, without improvement. Rapid digitalization again during the first three days in the hospital was ineffectual. The prognosis seemed extremely gloomy. Because of the very small urinary output, a catheter was inserted, and 250 cc. of residual urine discovered. An indwelling catheter was left in place, and constant drainage established. The following chart illustrates the miraculous restoration of compensation which occurred during the following three weeks:

Chart I (Case I.)—Note the change in cardiac rhythm from auricular flutter to auricular fibrillation to normal rhythm after bladder drainage was begun (indicated by the arrow). The fall of blood pressure and marked diuresis are represented.

After a rest period of two months, with constant bladder drainage, a prostatectomy was performed by Dr. S. Moorhead, and convalescence was uneventful. An electrocardiogram at this time showed a normal rhythm, some myocardial derangement, but with considerable improvement. For eight months the patient has remained compensated with a normal rhythm without the use of digitalis, and has again been able to carry on his work. This case is almost a counterpart of one reported by Davis[2] in 1928.

Case II.—G. H., a man, aged forty-three years, was admitted to the University Hospital, service of Dr. Stengel, with shortness of breath and edema. For two months prior to admission there had been increasing dyspnea and intermittent sharp precordial pain. Slight edema rapidly increased to anasarca. There was an indefinite history of nocturia and frequency. A summary of the positive findings follows: Delirium, orthopnea, cyanosis, slight exophthalmos, tremor, generalized edema, cardiac enlargement to the left, a rough systolic murmur at the apex not transmitted, auricular fibrillation, edema of the lung bases, and an enlarged liver.

The patient proved to be refractory to digitalis in large doses, both before admission and while in the ward. One week after admission, the bladder was found to be enlarged. The urinary tract was investigated and a dense stricture found in the bulbous urethra. This was dilated and a moderate residual urine discovered. A marked diuresis followed during the next four days, with complete disappearance of edema, and a gradual reduction in cardiac rate. Fibrillation reverted to normal rhythm after the use of quinidine. For six months the patient has remained compensated without digitalis, and is able to carry on his work.

In each case the urological picture was entirely eclipsed by the picture of severe cardiac failure. Insufficient attention was given to the urological history, for, in reviewing Case I, a history was later obtained of difficulty in voiding, diminution in caliber of the stream, and some dribbling of about two years' duration. In a review of Case II, there was a history of stricture requiring dilatation three years ago. Chronic rheumatic valvulitis and arteriosclerosis in Case I and hyperthyroidism in Case II were primarily considered as the factors precipitating myocardial insufficiency. I think, however, when one considers the poor response to rest and

digitalis, the tremendous diuresis immediately following the establishment of constant bladder drainage, the rapid recovery of compensation, and the continued freedom from cardiac manifestations, one is forced to conclude that the urological aspect of these cases is of primary importance in precipitating cardiac failure.

From a review of 40 cases of prostatic obstruction showing evidence of cardiac disease, carefully studied and followed during the past year, the following observations were made:

1. *Decompensation* occurred in 12 cases (30%). All except 3 were greatly improved following prostatectomy, and have remained compensated without the use of digitalis for an average period of six months. There was one postoperative mortality from cardiac failure in a patient with an abnormally low blood pressure. In the 2 remaining cases, although compensation was rapidly regained after bladder drainage and digitalization, death resulted from severe infection. These will be discussed later in the consideration of infection. Hypertension, ranging from 150 to 200 systolic and 90 to 110 diastolic existed in 9 of these 12 cases, and in 8 the blood pressure fell to normal after the relief of prostatic obstruction, and remained normal after operation.

2. *Auricular fibrillation* was found in 5 cases (13%). In 3 cases the rhythm became regular after bladder drainage was established, and has remained so. It was necessary to use digitalis in only 1 of these cases. The rhythm remained totally irregular after operative procedures in 2 cases.

3. *Partial heart block* occurred in 2 cases (5%). Conduction time became normal in 1 after bladder drainage, and in the other after prostatectomy. Digitalis was not used in either case.

4. *Extrasystoles* were numerous in 15 cases (38%), and completely disappeared with bladder drainage in all but 1 case.

In 22 of the 40 cases in this group (56%) cardiac arrhythmias were noted. Just why these arrhythmias should develop in such a large percentage of cases with prostatic obstruction is not adequately understood. However, when one considers that these cardiac irregularities disappeared in all but 3 cases, it seems indisprobable that there must be a definite relation between bladder retention and the functional properties of the heart.

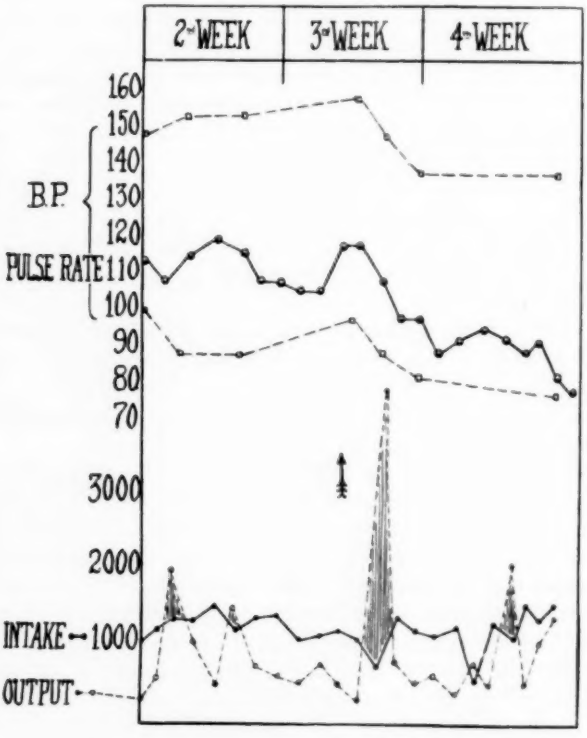
5. *Arteriosclerosis* was an outstanding finding in all of these cases. It occurred in an advanced, widespread form in 28 cases (70%). Retinal arteriosclerosis was prominent in 24 cases (60%). The most interesting feature was the occurrence of advanced coronary sclerosis in 4 of 5 cases examined at necropsy, and moderate coronary sclerosis in the fifth. There was extensive sclerosis with calcification of the mitral and aortic valves in 2 cases. The average age of these patients was sixty-seven years. In none was the blood pressure over 160 systolic and 90 diastolic. It would seem important to record the degree of coronary sclerosis in a large group of

cases with chronic prostatic obstruction, for if its occurrence is as common as found in these 5 cases, there is adequate reason why cardiac manifestations are present in such a high percentage of cases.

One other type of case, which is, in a way, related to those already discussed, should be briefly mentioned. Two cardiac cases with edema and without bladder obstruction had marked diuresis following the insertion of an indwelling catheter.

CASE III.—J. C., a man, aged sixty years, had had four mild attacks of decompensation, in the past seven years. Symptoms of decompensation with increasing edema brought the patient to the University Hospital. There was a past history of "rheumatism." Physical examination revealed marked cyanosis, orthopnea, rapid auricular fibrillation, loud systolic murmur

CHART II.



at the apex, cardiac enlargement to the left, blood pressure: 150 systolic, 100 diastolic, râles at the lung bases, enlarged liver, advanced arteriosclerosis, and generalized edema. The blood urea nitrogen was 30 mg. per cent. Two weeks of complete rest in bed, digitalization, and the use of diuretics, failed to restore compensation. Because the patient was not voiding freely, a residual urine determination was done. There was a residuum of 50 cc. of urine in the bladder. The bladder was dilated and atonic. A catheter was left in place and constant drainage established, and the bladder irrigated.

An unexpected and amazing diuresis followed, with complete disappearance of edema and recovery of compensation. The blood pressure and blood urea nitrogen dropped to a normal level. The following chart illustrates the results in this case:

Chart II (*Case III*).—Note the sudden and large diuresis which followed the insertion of an indwelling catheter (indicated by the arrow) and the corresponding fall of blood pressure and cardiac rate. Auricular fibrillation persisted.

Case IV.—E. M., a man, aged sixty-five years, gave a history of two attacks of pulmonary edema in 1929. Four weeks before admission the symptoms and signs of myocardial failure developed. On examination there was found cyanosis, dyspnea, cardiac enlargement to the left, frequent extrasystoles, arteriosclerosis, blood pressure: 144 systolic, 85 diastolic, râles at the lung bases, and moderate edema. Rest and digitalis were without effect. A fairly large residual urine was discovered, without any evidence of bladder obstruction. As in Case III, a marked diuresis followed the use of an indwelling catheter, and the edema disappeared within three days.

In each of these cases, there was found a residual urine without obstruction, and a very flaccid, atonic bladder. The diuresis, which followed adequate bladder drainage, was similar to the response obtained in the first 2 cases with bladder obstruction. No explanation is offered for this unusual response. It has been suggested that loss of bladder tone from passive congestion and confinement of the patient to bed for a considerable time might be factors. This called to mind a statement by Stutzin[3] that in certain hypertensive cases, bladder retention occurred without obstruction. The question was raised whether there might be a renorenal and a vesiculorenal reflex, as once described by Seres[4] and more recently by Muschat[5] to account for the diuresis following the use of an indwelling catheter.

These cases are added simply to stress the importance of a thorough investigation of the urinary tract in cardiac patients, and especially in those cases with edema which do not yield to adequate treatment.

Comment. Apparently no specific type of cardiovascular disease is produced by pathologic changes in the lower urinary tract. It seems important, however, that the definite relationship which obviously exists between the two, warrants a more thorough and detailed investigation, especially from its medical aspects.

This is particularly important because the clinician is often called upon to judge the prognosis for operation in these prostatic cases. On his judgment rests the vital question whether a patient should be condemned to a catheter life or risk operative procedures. I should like to mention three observations, in addition to the use of the electrocardiogram and the clinical tests for estimating cardiac reserve, which have proved to be of great prognostic significance:

1. The rapidity with which compensation is restored, either by digitalis or bladder drainage, is most important. In those cases in

which compensation is rapidly regained, regardless of the degree of cardiac failure, the operative prognosis is uniformly good. Case I is an admirable example.

2. The rapidity with which the blood pressure and blood-urea nitrogen returned to normal levels, is considered of prognostic significance.

3. The presence of an abnormally low blood pressure with evidence of cardiac insufficiency is thought to suggest a poor prognosis. This occurred in 2 of the 40 cases studied. At necropsy both had extremely soft, flabby hearts.

A great prejudice exists against the use of a catheter because of the fear of infection. It is true that urethral and bladder infections almost always follow the insertion of an indwelling catheter. However, the fear of this infection is less justifiable than is generally imagined. In the cases without edema minor grades of infection were encountered. These were found to be of no great significance. In cases with edema, where poor vascularity renders the tissues more prone to infection, a retention catheter was not used until compensation had been restored, unless the heart did not respond quickly to rest and digitalis. In those few cases where it was used in the presence of edema, infection was no more severe than in the cases without edema. I should like to refer briefly to the only 2 fatalities in this group resulting directly from infection. Both were cases of cardiac decompensation and moderately severe diabetes in which, because of the degree of prostatic obstruction, it was necessary to insert indwelling catheters. The edema disappeared rapidly in both cases, but death eventually resulted from severe infection. At necropsy, extensive hemorrhagic pyelitis and pyelonephritis were found in both cases. Six other diabetic patients with prostatic obstruction and without cardiac manifestations showed no abnormal tendency toward infection from indwelling catheters. Although this group of cases is small, the development of infection from indwelling catheters offered no serious complications, even in the presence of edema or diabetes. However, the presence of edema and diabetes together is a real danger signal.

Summary. There is a group of cases in which lower urinary tract obstruction and evidences of cardiac disease are commonly associated. That this may be of primary importance, from a therapeutic standpoint, is illustrated by clinical reports of 2 cases. The need of adequate urological histories and examinations in the medical studies on all male patients past middle life is emphasized. A brief statistical review of 40 cardiac cases with prostatic obstruction reveals cardiac arrhythmias in a large percentage of cases and widespread arteriosclerosis and coronary sclerosis of an unusually advanced type. Two cases are reported of myocardial failure refractory to rest and digitalis in which bladder retention without obstruction was discovered. The results of constant bladder

drainage as a therapeutic measure are discussed. The determination of prognosis in these cases and the evaluation of infection as a complication of catheter drainage are difficult problems which are briefly presented.

NOTE.—I wish to thank Dr. Alexander Randall, Surgeon-in-Chief of the Urological Division of the University of Pennsylvania, for his interest and assistance in this work.

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PAROXYSMAL VENTRICULAR TACHYCARDIA.

REPORT OF A CASE.

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PAROXYSMAL tachycardia of ventricular origin is no longer a medical curio. Since Lewis[1] published the first electrocardiographic records of a case of paroxysmal ventricular tachycardia in 1909, medical literature has had a generous contribution of case reports of undoubted authenticity, suggesting that the rarity of this arrhythmia is more relative than real. Relative because of our former, and often present, lack of adequate and convenient equipment for precise and exacting means for differentiating this type of tachycardia from similar cardiac irregularities.

Strauss,[2] in making a recent report on 2 new cases of paroxysmal ventricular tachycardia, gives an extensive bibliography on the 65 undoubted cases reported in medical literature to date and on half that number of cases in which the data presented did not entirely satisfy the accepted diagnostic criteria, although many of them are most likely cases of the arrhythmia.

The pathologic or causative disturbances responsible for the ushering in of the attacks of paroxysmal ventricular tachycardia are variable. The arrhythmia has generally been described as occurring in patients showing evidences of grave heart disease, in

most instances where there was disease of the coronary arteries.[3, 4, 5, 6] Also, on rare occasions this arrhythmia has been described as occurring in young people in whom the signs and symptoms of heart disease were entirely absent except those directly associated with the tachycardia, namely, precordial distress, palpitation, faintness, and mild dyspnea during the paroxysm.[7, 8, 9, 10] The prognosis is equally evasive depending almost entirely upon the major cardiac lesions.

This meager knowledge of the etiology of paroxysmal ventricular tachycardia justifies the recording of isolated cases, in the confidence that a larger series and more definite data will increase our perspective of this disturbance occurring in a relatively small number of hearts whose major pathology is similar and prevalent, or in which there are no evidences of serious heart disease.

Paroxysmal tachycardia is characterized by the sudden inception of an extremely rapid rhythm, of variable duration, and is usually of abrupt termination. The impulse governing the tachycardia arises in some area of the heart away from the sinoauricular node; that is, ectopic in origin. Paroxysmal tachycardia was first separated into that of auricular and that of ventricular origin by Mackenzie,[11] who concluded from a study of venous pulse tracings that the point of origin was not always the same. In ventricular paroxysmal tachycardia the cardiac acceleration arises from the production of abnormal stimuli in the ventricle.

Strong and Levine[12, 13] have described certain clinical criteria as an aid in differentiating ventricular paroxysmal tachycardia. "Although the heart rhythm is essentially regular, on careful auscultation distinct irregularities can be detected. This is in striking contrast to auricular paroxysmal tachycardia, in which the rhythm of the heart is absolutely regular. In the latter the sounds have a constantly similar character, whereas in the former the quality and intensity of the first sound at the apex is apt to vary with occasional heart cycles. The heart sounds for a period of several seconds may be identical when suddenly either a clicking sound is heard, a muffling, or an accentuation of the first sound takes place—not unlike the aucultatory findings in complete heart block."

Robinson and Herrmann[3] have already stated the electrocardiographic findings necessary to differentiate ventricular paroxysmal tachycardia from those of auricular origin. "The electrocardiogram must give definite indications that the cardiac impulses producing the high ventricular rate arise in the ventricles, and this is most clearly shown when a succession of auricular complexes can be made out occurring independently of and at a slower rate than the complexes of ventricular origin. The ventricular complexes are distinctly abnormal in form. The abnormal form of the ventricular complexes alone, however, cannot be taken as absolute proof that the impulses are of ventricular origin, as changes in form may be

caused by disturbances in intraventricular conduction. The presence of isolated ectopic ventricular beats before or after a paroxysm is regarded as evidence in favor of the tachycardia being of ventricular origin, especially when the form of the complexes of the isolated beats is the same as the form of the paroxysm."

Case Report. A well-developed and healthy appearing school boy, aged seventeen years, entered the University of Nebraska Hospital on July 26, 1929, complaining of frequent attacks of palpitation.

In 1926 the patient noticed attacks of irregularity of his heart action, especially when he became excited. He described the attacks, not as a rapid beating of his heart, but as an irregularity of his heart beat with occasional long pauses associated with the irregularity. His private physician prescribed digitalis and luminal—1-grain tablets of digitalis leaf three times a day for nine months, then twice a day for about fifteen months. This medication did not alter the attacks, which frightened him. Since undue excitement or strenuous work would usually precipitate an attack, in order to avoid them it became necessary for him to limit his activities and to resign himself to performing light work on the farm and attending school.

In March, 1929, the patient went to a medical clinic for observation. While at this clinic, the patient states, they found his heart entirely regular and advised him to omit all medication, which he did. His heart remained regular for two weeks, at the end of which time he had his first attack of palpitation. The attack came on suddenly while he was preparing to go to a class party, continued for about five minutes, and terminated abruptly. Following this he had frequent attacks of palpitation, as often as three to four times a day, varying from a few minutes to several hours in duration. Undue excitement would precipitate an attack which always terminated abruptly.

Three weeks before entrance to the hospital he had had a sudden fainting attack. He had been plowing corn for three days previous to this date and had not been feeling well—he was constipated and troubled with "gas in his stomach." He states that he lost consciousness, his lips became blue, and he vomited. He does not know what occurred during the following twelve hours except that his mind would momentarily become clear but objects about him appeared hazy and blurred. He felt nauseated and vomited several times. Following this episode the attacks of palpitation became more frequent and they would often continue throughout the entire night but with no subjective symptoms except the uncomfortable sensation of his heart beating rapidly.

There was no history of sore throat, rheumatism, chorea, diphtheria or scarlet fever. As a child he could run and play as hard as the other children in school. His teacher, however, had on several occasions remarked to his parents that he became unusually short of breath. He stated that he had always been shy and nervous in school and had a constant fear of recitations and examinations to a degree which he himself considered abnormal. He had never used tobacco or alcohol in any form.

Physical Examination. The physical examination revealed a well-developed and well-nourished individual who was apparently very little disturbed by his paroxysms. At the time of his entrance into the hospital he was having repeated attacks of tachycardia, usually initiated when he assumed a reclining position. The attacks began suddenly and terminated abruptly but were unassociated with subjective symptoms except a shortness of breath on exertion and a slight feeling of oppression over his precordium. The tonsils were small and cryptic, but not inflamed. The lungs

and abdomen were normal. There was no cardiac enlargement by percussion, and this was confirmed by Roentgen ray. The heart sounds were regular except during the paroxysms and directly following them. There were no evidences of valvular heart disease. All laboratory tests of the urine and the blood were normal.

During the paroxysm the heart sounds became very rapid but regular. There was a cyclic accentuation of the first sound at the apex; that is, a loud beat followed by two, three, or more beats of lesser intensity and then another louder beat, thus repeating the cycle. The pulse, as accurately

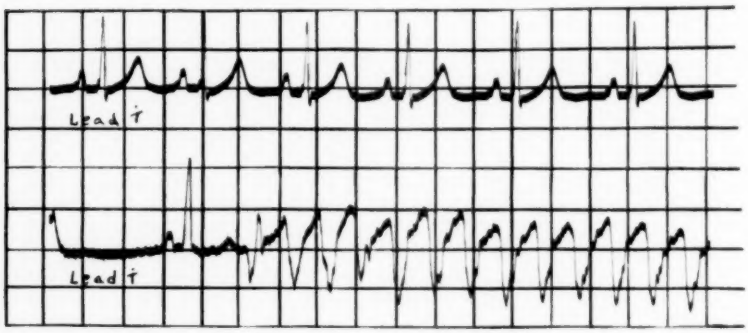

FIG. 1.—(Case 29196) July 26, 1929. Upper record shows the normal sinus rhythm. The lower record was taken at the inception of an attack of paroxysmal ventricular tachycardia. Time intervals expressed in $\frac{1}{4}$ or 0.25 seconds in this and succeeding records.

as it was possible to count it at the wrist, varied between 80 to 90 per minute. His lips were slightly cyanotic. His only subjective symptoms were a vague feeling of oppression over his precordium and shortness of breath on exertion. He had never experienced cardiac pain with the paroxysms. Vagal stimulation and ocular pressure were ineffective in terminating the paroxysm. The paroxysms stopped abruptly and there followed a shower of extrasystoles with long compensatory pauses and a pulse rate as low as 30 per minute. The pulse rate became normal with the disappearance of the extrasystoles. Roentgen ray taken during a paroxysm showed some ventricular enlargement to the right.

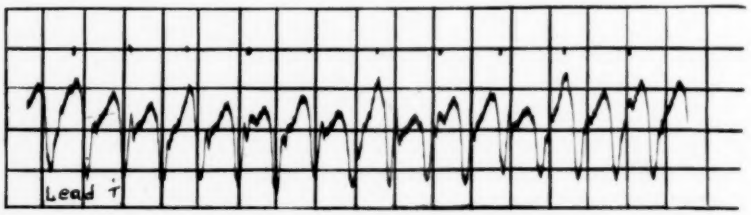

FIG. 2.—(Same case) July 26, 1929. A continuation of the above lower record. Notice the succession of auricular complexes occurring independently of the complexes of ventricular origin.

Electrocardiograms taken at the inception and the termination of an attack showed a typical paroxysmal tachycardia of ventricular origin. The tracings satisfy all the requirements mentioned by Robinson and Herrmann[3] for the diagnosis. The ventricular complexes are highly abnormal in form. Directly following the inception of the paroxysm (Fig. 1) a succession of auricular complexes (Fig. 2) can be made out occurring inde-

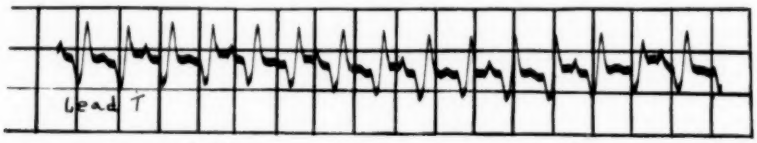

FIG. 3.—(Same case) July 26, 1929. This record shows the continuation of the above paroxysm taken ten hours after its inception. The patient had fallen asleep. Notice that an auricular complex occurs after every second ventricular beat.

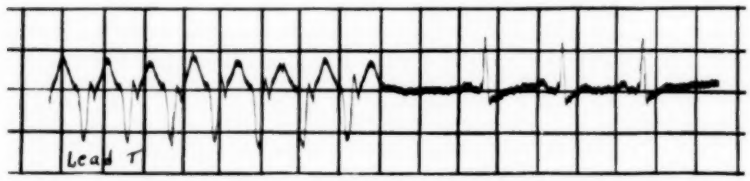

FIG. 4.—(Same case) July 28, 1929. Notice the abrupt termination of the paroxysm is followed by a definite pause.

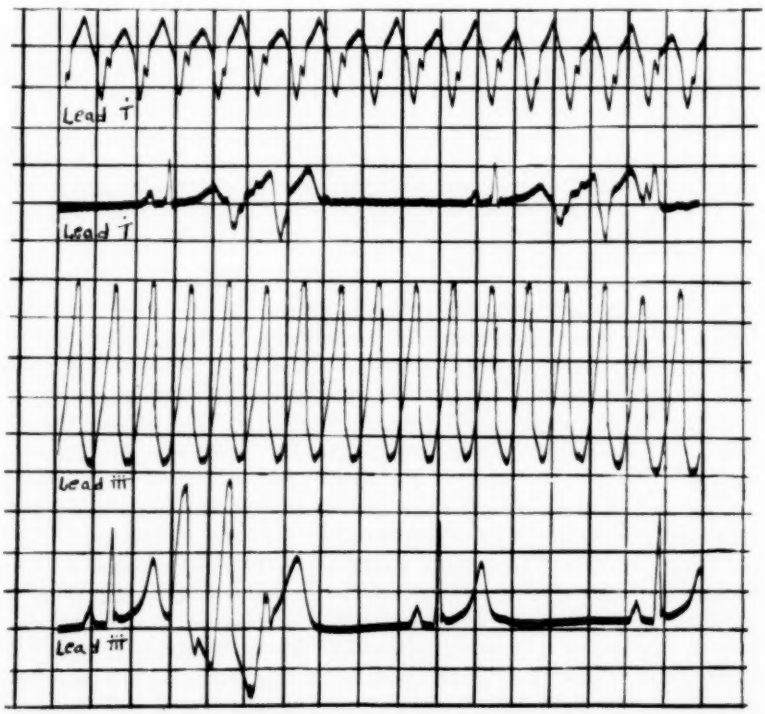

FIG. 5.—(Same case) August 2, 1929. Showing records of Leads I and III taken during a paroxysm. Also records of Leads I and III directly following the paroxysm. Notice the interruption of the normal sinus rhythm by complexes of ventricular origin similar in form to the paroxysm.

pendently of and at a slower rate than the complexes of ventricular origin, that is, the auricles are contracting independently from the ventricles. As the paroxysm continues (Fig. 3) the auricular complexes occur after every second ventricular beat, the rate of the ventricles being 220 per minute and that of the auricles one-half this rate, that is, the auricles are responding to reversed impulses from the ventricles. Similar curves, in which the auricles beat at exactly half the rate of the ventricles, have been published by Marvin and White[7] and by Robinson and Herrmann.[3] The paroxysm was followed (Fig. 4) by a definite pause, then a period during which the slow supraventricular beats were interrupted by ectopic beats of ventricular origin (Fig. 5) similar in form to the beats which compose the succeeding paroxysm.

With a daily dosage of 1 gm. of quinidin sulphate, administered by mouth in 3 equal doses, the paroxysms were entirely controlled and the patient left the hospital with instructions to vary the dosage as necessary. He returned in three months stating that he was able to entirely control the attacks by taking 5 grains of the quinidin in the morning and in the evening. If, however, he omitted one dose he would invariably have an attack. He also observed that after taking the quinidin orally it required about forty-five minutes for it to become effective. This corresponds with the case reported by Scott[14] where a single dose —0.4 of a gram of the drug — invariably terminated the paroxysm in from thirty minutes to one hour after given by mouth.

The patient again returned for examination on May 1, 1930. Although his private physician had removed his tonsils two months previously, he had noticed no change in his suspectibility to paroxysmal attacks during the interim. He still required 5 grains of quinidin in the morning and in the evening in order to be entirely free from the attacks. The patient omitted the quinidin for the eighteen hours preceding his visit and he was able to initiate short paroxysms by moderate exercise. The electrocardiograms at this time showed, by the configuration of the ventricular complexes, that the same ectopic focus in the right ventricular base was responsible for the paroxysms. The extrasystole phenomenon following the paroxysm had entirely disappeared.

Levine and his coworkers[12, 13] have emphasized the varying quality of the first heart sound at the apex in different cycles during paroxysmal ventricular tachycardia, which is in striking contrast to the constantly similar character in the quality and intensity of the first sound in paroxysmal auricular tachycardia. Cushny and Grosh[16] (their Fig. 15) have shown that if the auricular contraction occurs before the ventricle is completely relaxed, there is a certain degree of obstruction to the outflow of the blood from the auricle resulting in a larger wave than usual in the jugular tracing. The next auricular systole occurs when the ventricle is relaxed; the inflow is freer, and the wave in the jugular is correspondingly smaller. This experiment shows the important fact that the auricle must contract at a very definite point in the ventricular cycle if the optimum efficiency of the heart is to be attained. The comparatively slight displacement in the auriculoventricular rhythm is sufficient to cause marked anomalies, not only in the jugular pulse but also in the filling of the ventricle during diastole. Lombard and Cope[17] have shown (their Fig. 9) that the period of diastasis

rapidly lessens as the heart cycles shorten, and consequently that the period of rapid filling, and the filling caused by the contraction of the auricles, becomes of greater and greater importance as the heart rate becomes more rapid.

In paroxysmal ventricular tachycardia, as in the case reported here, where the ventricular rate varies between 220 and 250 per minute, the heart cycle would vary between 0.272 and 0.24 seconds and the period of rapid ventricular filling would be extremely short. In Fig. 2 the auricles and ventricles are beating at independent rhythms (auricles 150 per minute and ventricles 250 per minute), and it is evident that the occasions upon which the auricles would contract at the moment of ventricular diastole would be variable. However, on these occasions there would be a greater ventricular filling. With this increased ventricular filling one would expect a change in the quality and loudness of the first sound at the apex and, at the same time, a change in the quality of the radial pulse. Thus the slight displacement in the auriculoventricular rhythm in paroxysmal ventricular tachycardia is sufficient to cause the cyclic accentuation of the first sound at the apex.

The absence of extrasystoles, following the use of quinidin in this case, was of interest in view of the fact that upon the patient's first visit to the hospital there were numerous extrasystoles both preceding and following the paroxysms; and it was possible to elicit, with exercise, isolated extrasystoles without an associated paroxysm. With the administration of quinidin sulphate in maintenance dosage, the extrasystole and paroxysmal phenomena were entirely controlled. When one single maintenance dose of the drug was omitted, it was possible, with exercise, to initiate typical paroxysmal attacks without the associated extrasystoles. That is, there was a period following the discontinuance of the quinidin during which the paroxysmal attacks were readily elicited by exercise, but the associated or isolated extrasystoles were entirely absent. This absence of the extrasystole phenomenon would seem parodoxical if we are to believe that the only difference between extrasystoles and the tachycardia lies in the multiplicity and successive nature of the latter.

Lewis[4] produced ventricular extrasystoles and ventricular tachycardia in animals by ligating the coronary arteries, more especially the right, subsequent to complete section of both vagosympathetic nerves. He concluded that such a tachycardia was produced as the result of a change intrinsic in the heart, a tachycardia which can in no way be attributed to central influence. The extrasystoles precede or follow the tachycardia. Clinically[15, 18] and experimentally[19] there is sufficient evidence to show that both may arise out of the administration of digitalis, being due to a hyperirritability of the ventricles. Furthermore, a continuous and rapid action of the dog's ventricle can be produced by rhythmically stimulating the

organ with induction shocks. The organ is driven rhythmically and rapidly for a few seconds, the stimuli are then abruptly withdrawn, whereupon the ventricles usually continue in a state of fibrillation. However, in a certain proportion of such experiments a rapid and regular action of the ventricles continues for a brief or longer period of time after stimulation has ceased and then terminates abruptly with the establishment of normal sinus rhythm, thus simulating ventricular paroxysmal tachycardia.

If, from these points of similarity between ventricular extrasystoles and paroxysmal ventricular tachycardia, we conclude that the tachycardia is merely the expression of a more serious form of extrasystole phenomenon (that is, a rapid succession of multiple extrasystoles arising from an area of hyperirritable ventricular musculature), and that the difference lies in the rapidity of the impulse formation rather than in the mechanism of the formation of the impulses, we would expect the quinidin to depress the area of hyperirritability to a point of slower impulse formation simulating rapidly occurring but isolated extrasystoles; we would expect to elicit a gradation of difference between the tachycardia and the extrasystole phenomena. However, this does not occur. When the quinidin is discontinued, the paroxysmal attacks reappear and terminate abruptly unassociated with and unaccompanied by isolated extrasystoles. It would be only fair to conclude, from the fact that the extrasystole phenomenon is more easily depressed by the quinidin than is the paroxysmal phenomenon, that the difference lies in the mechanism of the impulse formation rather than in the degree of hyperirritability or simple rapidity of impulse formation.

Lewis' conception of a circus movement in the auricle producing auricular fibrillation and auricular flutter is widely accepted—*cadit quæstio*. It has been suggested that a similar mechanism is responsible for ectopic tachycardia in the ventricles. Palmer and White[5] favor the idea that a circus movement may be responsible for the paroxysmal tachycardia of ventricular origin, the path of the circus varying somewhat from time to time as it does to a lesser degree in auricular flutter, thus accounting for the variation in time and also in the shape of the abnormal ventricular complexes.

In 1914 Mines and Garrey reported that they had obtained circus movements in rings of muscle cut from the turtle ventricle. That a circus movement can remain within a relatively fixed and uniform path when traveling around the contractile bell of the jelly fish, or a ring of muscle cut from the dog's ventricle or auricle, or the circular auricular muscle which surrounds the superior and inferior vena cava, is universally accepted. Is it possible for such a movement to exist in the complex syncitium of the main mass of normal auricular or ventricular musculature? If circus movement began in a circle of normal heart muscle *in situ*, the varying paths through

which this circus could, and undoubtedly would, move is infinite and the ventricular rhythm would become irregular. Viewing a dog's heart, in which ventricular fibrillation has been produced, we find that the condition certainly simulates a moving circus.

If the circus movement is the mechanism by which paroxysmal ventricular tachycardia is produced, we must admit that the path through which the circus passes in an individual heart is relatively fixed. Electrocardiograms taken during different attacks in the same individual show a fairly constant uniformity in the construction of the ventricular complexes, that is, the ectopic focus responsible for the abnormal rhythm is the same in each attack. A definite area in the myocardium has become vulnerable or hyperirritable. Where there is clearly some interference in the coronary circulation the hyperirritability may be explained by the resulting localized anemia of the cardiac muscle. In digitalis we have a direct stimulating action on the heart muscle, that is, an increase in the irritability of the myocardium. In the absence of either of these two factors we must look for some congenital anomaly or neuromuscular aberration which would cause a fixed area in the myocardium to become vulnerable. In the case I have reported here the ectopic focus responsible for the paroxysmal tachycardia is located in the right ventricular base. Records taken at three-month intervals show no essential alteration in the form of the ventricular complexes. Therefore, it would be fair to conclude that all his paroxysmal attacks took their origin from the same focus.

The first attacks of cardiac irregularity described by the patient can only be interpreted as that of extrasystoles or extremely short runs of paroxysmal tachycardia. The attacks had a definite relationship to exercise and emotional disturbances. His typical attacks of paroxysmal tachycardia did not occur until after a long course of digitalis therapy followed by a period during which he received no medication. It is very improbable that the digitalis was a direct cause of the paroxysmal attacks in this case. There was no change in his cardiac irregularity during the period he was taking the digitalis, and the typical paroxysmal attacks did not occur until two weeks following the discontinuance of the drug. The paroxysmal attacks were also definitely influenced by exercise and psychic disturbances.

That the heart is capable of extreme variation in its activities as the result of emotional stimulation, mechanical or metabolic disturbances, combined with an increased demand on the work of the heart, is well recognized in cases of "cardiac neurosis." Is a heart, in which there is no demonstrable disease, either in its muscular, valvular or conduction mechanism, and in an individual not the subject of disease elsewhere, capable of activating so grave a form of ventricular tachycardia as an expression of shunted emotional outlet? Or are we here dealing with a heart in which there is some

preëxisting congenital anomaly or neuromuscular aberration which is favorable to the production of the circus movement, but too delicate to be demonstrated by our present means of precision, and yet abnormally sensitive to emotional stimulation and increases demand on the work of the heart?

Conclusion. 1. A case of paroxysmal ventricular tachycardia in whom there is no evidence of serious heart disease is reported with electrocardiographic records.

2. The slight displacement in the auriculoventricular rhythm in paroxysmal ventricular tachycardia is sufficient to cause the cyclic accentuation of the first sound at the apex.

3. It is suggested that in paroxysmal ventricular tachycardia occurring in an individual—not the subject of demonstrable heart disease—we may be dealing not only with an inherited sensitive nervous system but also with an inherited cardiac neuromuscular aberration.

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THE PROGNOSTIC VALUE OF THE SEDIMENTATION RATE IN ARTHRITIS. A MODIFICATION OF THE TECHNIQUE.

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The rapidity of the sedimentation of the red blood cells in the plasma of the sick, known to Hippocrates, carefully observed and described by Galen, received its first scientific scrutiny by John Hunter in 1767. This great physician and teacher of the early eighteenth century delved deeply into the significance and possible causative factor for this phenomenon. He was able to demonstrate by simple and ingenious tests and observations that this agent was not centered in the erythrocyte, as had been advocated prior to and during this period, but in some element present in the plasma of the patient. By these findings he was able to establish a definite relationship between the amount of sedimentation and the severity of the infection. The splendid work of Hunter was continued for some time by J. Müller, Davy and others, but then vanished almost completely until the middle of the nineteenth century. Then, it reappeared as the subject of numerous lectures and publications. Although considered a procedure of worth, it for some unknown reason again was discarded, not to be heard of until 1917, when it was rediscovered and reappeared as a diagnostic test for pregnancy. Since its revival by Fahraeus and its introduction as an accurate laboratory test, it has captured the attention of the medical profession the world over, and is at present enjoying its greatest popularity.

Technique. Since the introduction of this simple test in 1917, numerous modifications have been suggested and employed. All of these methods, however, can be classified under two main procedures. The first is the original Westergren-Fahraeus method, which is used to determine the amount of sedimentation that takes place during a specified period of time. The second, the Linzenmeier method, on the other hand, notes the length of time required for a red blood cell column to drop a specified distance to an indicated point. All methods require a specified amount of blood, usually obtained by puncture of the median cephalic vein. This blood is drawn into a syringe containing sodium citrate (3.5 to 5%) in the proportion of 1 part citrate and 4 parts blood. After thorough mixing, its contents are emptied into a calibrated tube. In the Fahraeus method the amount of sedimentation below the 20 cm. point is measured at the end of one hour. In the Linzenmeier the time needed for the column to drop from the top to a point 18 mm. below is noted. It was while using both of these methods that I found that each procedure had certain drawbacks and that some method utilizing the good points of each might be used.

The method I have employed is essentially the same as the original Fahraeus, except for the measuring instrument. By venupuncture 1.6 cc. of blood is drawn into a syringe containing 0.4 cc. of a 3.5% solution of sodium citrate. The piston of the syringe is then drawn back slightly and its contents mixed thoroughly. The mixture is then emptied into the sedimentation cylinder (Fig. 1). At the end of forty-five minutes a reading

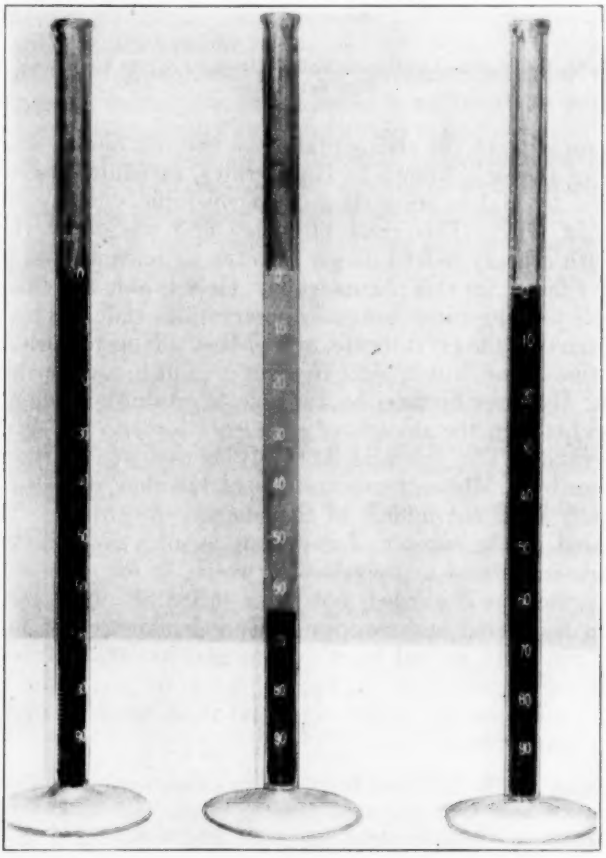

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FIG. 1.—(1) Sedimentation tube with blood column immediately after filling. (2) Sedimentation tube after three-quarters of an hour in case of acute rheumatic fever. Shows rate of 64.5%. (3) Sedimentation tube after three-quarters of an hour in normal individual. Shows reading of 3%.

is made. This cylinder is constructed to hold 2 cc. The calibrated column is 113 mm. long, 5 mm. inner diameter, and is subdivided into 100 equal parts. Thus the readings can be made directly in percentage. As a rule a fine capillary tube slightly longer than the cylinder is put inside and the blood mixture emptied alongside it. This ensures perfect mixing, and facilitates filling and emptying of the cylinder. This tubing is removed gradually as the blood column rises in the calibrated tube. The normal reading is 3 to 5 per cent in forty-five minutes.

Theories. The accelerated sedimentation of the red blood cells in the plasma of patients suffering with acute infections is a non-specific biologic phenomenon present whenever the blood stream receives the products of cellular disintegration. The immediate cause of the agglutination and the falling out of the red cells from their suspension was long in the dark. With investigations in

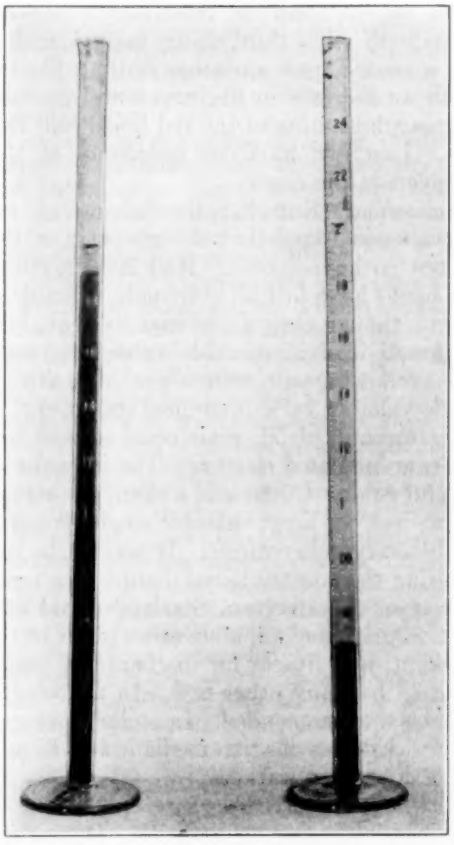

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FIG. 2.—(4) Sedimentation cylinder in case of acute leukemia, with severe anemia. Note the three subdivisions, the small upper section of clear plasma, the intermediate gray column of leukocytes and the lower section of red blood cells. (5) Sedimentation cylinder in case of acute infectious arthritis. Reading shows rate of 75.5%.

electrophysical and chemical aspects of the blood much of this obscurity was cleared. At present there are five theories that are presented to explain this reaction. The first, that propounded by Höber and Mond, is an electrophysical interference with the blood electric current, loss of potential or conductivity associated with serum globulin changes. The second and probably most acceptable

theory is that sedimentation is caused by serum-fibrin changes in the blood. The acceleration is accounted for as a protein phenomenon originating in a disturbance in the albumin-globulin-fibrinogen ratio. Linzenmeier, Höber and others have found that the addition of fibrinogen, protamin histone, and so forth, caused an increase in sedimentation due to a decrease in the negative charge of the erythrocytes. Gram, analyzing the fibrin content of 542 plasmas, found an increase in infectious diseases, pregnancy, nephritis, and so forth. The third theory maintains that accelerated sedimentation is caused by a variation in the colloidal stability of the serum, with an increase in fibrinogen and globulin concentrations. The autoagglutination of the red blood cells as a theory has few adherents. Last, we have an imbalance of the cholesterol lecithin ratio given as the cause.

Clinical Application. Entering the laboratory as a test for pregnancy, it was soon found that though positive, the sedimentation test was not pathognomonic. Had investigations stopped at this point we should have lost an extremely valuable aid. Linzenmeier and others, though they discovered its negligible significance in pregnancy, found it of inestimable value in gynecologic conditions. Surgeons following suit, were also able to attest to its differential diagnostic value in various surgical conditions. Thus, where normal temperature and blood count often seemed to mislead, the sedimentation rate indicated caution. The internist also hastened to use this helpful guide. Cutler and Cohen, reporting on 500 chest cases, found this test the most valuable single means of estimating activity of pulmonary tuberculosis. It was to be of incalculable value in measuring the constitutional disturbance produced by the tuberculous process. Westergren, Starlanger and others consider the sedimentation test more valuable as an index of the course and value of treatment, and fitness for discharge of patients suffering with tuberculosis, than any other test. In neurology its frequent application has been recommended. In otolaryngology it was found of marked value. In cases of otitis media it acts as an indicator for operation, or possible complications.

For the past two years I have been interested in the sedimentation rate and its application in cases of arthritis. During this time I was able to follow throughout their courses 150 cases of acute rheumatic fever, and 25 cases of infectious arthritis. Sedimentation tests were taken at first twice a week and later only once a week. Blood counts, chemical tests, blood cultures and other pertinent laboratory procedures were employed when deemed necessary. In a series of comparative cases, readings were noted every five minutes, to determine whether curves produced varied and might be specific for those conditions. Graphs were plotted to determine whether the character of the curves produced might disclose the presence or threatening approach of some complication. Below I have given a résumé of a few of the representative cases of this interesting group.

Case Reports. CASE I.—M. M., aged fifteen years, was admitted with the diagnosis of acute arthritis. His chief complaints were pain, redness and limitation of motion of the right knee. One year ago patient had had an attack of rheumatic fever with pain in all joints. After a three-day period of fever and profuse sweats, patient recovered. During the interval between this attack and six weeks before admission, patient had occasional joint pains, and would tire easily. About six weeks ago patient had sudden swelling and redness of the right knee and ankle. This was accompanied by neither pain nor temperature. During this period he also developed a facial edema. Facial edema and swelling of the right ankle disappeared about three weeks ago when the right knee became very painful. Patient has had no dyspnea, palpitation or precordial pain. For the past two weeks he has had five to six bowel movements daily. During the course of his illness he has lost 15 pounds.

General appearance is that of a poorly developed, poorly nourished, very anemic youngster who appears chronically ill. Face is somewhat edematous and shows some phlebectasia. Entire musculature wasted and flabby. Local condition shows a circumscribed swelling around the right knee extending above the patella. There is definite fluctuation, but no tenderness, redness or marked limitation of motion.

Patient upon admission had a temperature of 99, pulse of 90 and respirations of 26. He weighed 80 pounds and had a blood pressure of 140 systolic and 70 diastolic. From the date of his admission to day of exitus fifteen weeks later temperature showed nothing unusual. Roentgen ray of chest showed no infiltration or consolidation in either lung, no tuberculosis. There is thickening of pleural fissure as well as the parietal pleura. Heart shows slight enlargement with accentuation of the right auricle and pulmonary artery. Roentgen ray of sinuses shows thickening of the mucous membranes. Roentgen ray of right knee shows effusion extending into the quadriceps and extensor tendons. Later plates showed intercondylar bone destruction, with atrophy of the bones of the right knee joint suggestive of tubercular involvement. Last plate showed articular surfaces of tibia and fibula in contact, patella displaced downward. There is considerable infiltration of the soft tissue, and effusion. Chest plate shortly before exitus showed right bronchopneumonia. Electrocardiograph showed simple tachycardia. Treatment during the patient's stay in the hospital included salicylates orally, rectally and externally, daily diathermy, plaster casts, arthrodesis of the right knee and finally repeated blood transfusions.

Laboratory Data: Urine: Sp. gr. between 1008 to 1012, albumin negative to 3+; microscopic—moderate hyalin casts; P.S.P.—15% first hour, 15% second hour. Blood cultures, repeatedly negative. Wassermann test, negative. Blood chemistry: glucose, 84 mg.; N.P.N., 26 mg.; calcium, 11.6 mg.; cholesterol, 296.2 mg.; total protein, 4.43; albumin, 1.97; globulin, 2.46; ratio, 0.8.

Blood counts: May 25.—R. 3.61, Hb. 40, W. 11,000, St. 4, S. 64, B. 1, E. 3, Ly. 24, Mo. 4

June 6—R. 2.25, Hb. 39, W. 16,400, Mt. 1, St. 9, S. 71, Ly. 18, Mo. 1

Aug. 21—R. 1.84, Hb. 32, W. 21,600, St. 2, S. 78, E. 4, Ly. 12, Mo. 2

There is very marked anisocytosis, poikilocytosis, polychromatophilia, 3% normoblasts, 465,000 platelets; coagulation time, two minutes; bleeding time, three minutes; clot retraction, normal. Sedimentation tests taken during the early part of the patient's stay, and those taken toward the end showed a maximal amount of 85% in thirty minutes. Patient died and the *autopsy* findings were: bronchopneumonia, chronic pleurisy with acute exacerbation, pseudomembranous bronchitis, albuminous degeneration of the liver, amyloid degeneration of the spleen, kidneys and adrenals, necrosis of the pancreas, and enteritis.

CASE II.—G. S., aged eighteen years, was admitted on the medical service on May 24, complaining of joint pains for over a period of nine days. About twelve days ago patient felt out of sorts, had chilly sensations, vague aches and pains over the entire body, sore throat and slight cough. Finding his temperature to be 103° F., he took to bed. Three days later he developed pain and swelling of the right wrist with marked limitation of motion. He then suffered with a migratory involvement of the opposite wrist, knees, ankles, shoulders and then the fingers. During this period he perspired profusely.

Physical examination revealed a well-developed, well-nourished male aged eighteen years, with marked facial pallor, looking acutely ill. Chest showed systolic murmur at the apex. Involved joints were stiff, slightly tender, motion somewhat impaired. Admission temperature of 104° F. dropped by lysis, and all joint symptoms disappeared after four days of intensive salicylate therapy.

Roentgen ray of chest showed cardiac configuration of mitral stenosis. Roentgen ray of joints negative.

Laboratory data: Urine, 1010 to 1020, faint trace of albumin, occasional hyalin casts. Blood cultures, negative; Wassermann, negative; blood chemistry: glucose, 135 mg.; N.P.N., 27.5; uric acid, 3 mg.

Blood counts: April 25.—R. 3.73, Hb. 71, W. 16,000, St. 4, S. 79, Ly. 8, Mo. 7, E. 0
May 1.—W. 10,600, St. 4, S. 73, Ly. 17, Mo. 6
May 10.—R. 3.87, Hb. 65, W. 9,600, St. 1, S. 63, Ly. 29, Mo. 7
May 12.—R. 4.13, Hb. 67, W. 10,700, St. 3, S. 73, Ly. 17, Mo. 4, E. 3
July 1.—W. 9,000, St. 1, S. 63, Ly. 30, Mo. 5, E. 1

Sedimentation rates: April 25, 62%; 29, 60%; May 5, 40%; 13, 6%. Discharged May 15. July 1, 4%.

This case is one of acute rheumatic fever. It is interesting to note that the sedimentation rate on admission was 62%, and although the temperature and symptoms disappeared four days later, the rate remained at that height. Although symptom-free, the sedimentation rate did not reach normal until three weeks later. On patient's return for observation seven weeks later, his sedimentation rate was normal. During this interval he had been absolutely symptom-free.

CASE III.—E. K., male, aged forty-nine years, was admitted with chief complaint of polyarticular pain. Eight days prior to admission he had developed an acute attack of throbbing pain and swelling of the left ankle. On subsequent days the left wrist, right ankle, and left elbow were involved. Ten years ago he had had a similar attack which lasted six months, and one four years ago which lasted eight weeks. Entering with a temperature of 101.4° F., pulse, 100, respiration, 34; he maintained a low-grade temperature during his seven-and-a-half-week stay in the hospital. The patient was discharged slightly improved. All Roentgen rays were negative except those of the joints, which showed a productive arthritic involvement of the bones of the wrist, knees and ankles; also of the tarsal joints of the left foot.

Laboratory Data: Urines: Specific gravity between 1008 to 1030, with occasional faint trace of albumin, and occasional hyalin casts. Blood cultures, negative; Wassermann, negative; gonococcus complement fixation, negative; chemistry: glucose, 111 mg.; N.P.N., 35 mg.; uric acid, 3 mg.; calcium, 9.4 mg.

Blood counts: April 14.—R. 4.42, Hb. 85, W. 15,200, St. 4, S. 60, E. 4, Ly. 26, Mo. 6
May 7.—W. 8,000, St. 3, S. 69, E. 1, Ly. 20, Mo. 7.
May 22.—W. 7,000, St. 5, S. 60, E. 2, Ly. 27, Mo. 6
July 1.—W. 9,500, St. 4, S. 62, E. 1, Ly. 26, Mo. 7

Sedimentation rates: April 18, 32%; 29, 52%; May 7, 60%; 15, 37%; 22, 45%; 31, 25%. Discharged June 1, 1930. July 1, 39%.

This case of infectious arthritis gives a history of two previous attacks. It is extremely difficult to venture an opinion as to whether both of these attacks were rheumatic, or arthritic manifestations secondary to some focus of infection. Are we dealing now with a case of acute arthritis deformans? Obstinacy toward all types of treatment, low-grade temperature, tendency toward chronicity with periarticular changes make this a possibility. However, since arthritis deformans is at present being considered secondary to some infection, the classification of acute infectious arthritis for this case will hold. The sedimentation rates clearly demonstrate that the patient's condition was aggravated during the first three weeks, and then gradually returned to a basic low-grade level. Upon return for observation one month later, he still had all of his old complaints, walked with difficulty, could not clothe or feed himself because of stiffness of both hands. The sedimentation rate was same as on admission.

Case IV.—I. K., lawyer, aged twenty-four years, was admitted with the chief complaint of joint pains. During the past winter he had had frequent coughs. One week ago he had an attack of pain in the left knee and temperature. Local applications caused improvement, but he nevertheless soon developed soreness in the left hip and ankle. On the following day joints of the opposite side were affected. At no time did he notice any swelling, redness or limitation of motion. Four days later he noticed swelling and pain in the right big toe. Physical examination was negative except for a blowing systolic murmur at the apex transmitted to the axilla, and also a soft blowing diastolic murmur at the apex. P2 accentuated.

Roentgen ray of chest showed cardiac shadow enlarged, mitral configuration. Joints, negative.

Laboratory Data: Urine: specific gravity, 1015 to 1032, very faint trace of albumin, occasional hyalin casts; blood cultures, negative; Wassermann, negative; blood chemistry: glucose, 138 mg.; N.P.N., 25 mg.; uric acid, 2.8 mg.

Blood counts: April 2.—R. 4.09, Hb. 74, W. 10,700, St. 5, S. 73, E. 1, Ly. 15, Mo. 6

April 28.—R. 4.21, Hb. 76, W. 6,800, St. 7, S. 54, E. 1, Ly. 32, Mo. 4

May 8.—R. 4.28, Hb. 78, W. 4,800, St. 2, S. 57, E. 2, Ly. 37, Mo. 2

July 1.—W. 7,000, St. 2, S. 49, E. 0, Ly. 45, Mo. 4

Sedimentation rates: April 10, 37%; 17, 25%; 26, 12.5%; May 9, 9%; July 1, 2.5%.

In this case of articular rheumatism, we also find the curve of the sedimentation rate lagging perceptibly behind the rapid improvement in physical signs and symptoms. Examination seven weeks after discharge shows sedimentation rate normal, patient with no subjective or objective complaints.

Case V.—E. B., female, married, was admitted with the provisional diagnosis of acute rheumatic fever. Her chief complaints were swelling of the hands and feet for the past five days; fever, profuse sweats and generalized pains for two days. Patient had some adnexal operation twelve years ago. Four days before admission patient suddenly developed severe pains in the right hand and a temperature of 103° F. Right hand became markedly swollen, and two days later right foot was similarly involved. During this period she has felt very weak, has perspired profusely, has had elevated temperature, but no chills. Physical examination reveals young woman of thirty looking acutely ill. There is a systolic murmur inside the apex beat, P2 equals A2. There is tenderness to pressure in the right lower

quadrant. Both elbows show marked limitation of motion. Left hand and right foot are markedly indurated and swollen. Both wrists are swollen and tender. All affected joints have limited motion. Roentgen ray of hands and feet shows no evidence of bone destruction or infiltration. Heart is generally enlarged and has a mitral configuration. Patient was given salicylates in large doses orally and by rectum, but without any influence or relief of symptoms. Other medications, typhoid and gonococcus vaccines, and physiotherapy were employed with similar lack of effect.

Laboratory Data: Urine: specific gravity, 1004; trace of albumin; occasional red blood cells; cervical smear negative for gonococcus; Wassermann, negative; gonococcus fixation, negative; blood chemistry, negative.

Blood counts: June 6.—R. 3.65, Hb. 62, W. 11,000, St. 4, S. 78, E. 1, Ly. 10, Mo. 7
June 26.—R. 3.97, Hb. 64, W. 6,200, St. 9, S. 67, E. 1, Ly. 15, Mo. 8
July 1.—R. 3.4, Hb. 63, W. 11,000, St. 7, S. 80, Ly. 8, Mo. 5
July 14.—R. 3.69, Hb. 59, W. 5,200, St. 5, S. 66, E. 1, Ly. 19, Mo. 6, B. 1, My. 2
July 23.—R. 3.5, Hb. 61, W. 5,400, St. 6, S. 62, E. 0%, Ly. 20, Mo. 8, B. 3, My. 1

Sedimentation rates: June 30, 64%; July 7, 69%; July 11, 65%; July, 17, 67%; July 23, 67%; July 30, 69%; August 19, 72%.

Symptoms, signs and sedimentation rate made the provisional diagnosis most plausible. However, when it was found that patient did not show any signs of improvement with intensive salicylate therapy and the sedimentation rate showed no tendency to fall, the diagnosis of infectious arthritis became paramount. The possibility of a Neisserian polyarthritis was considered because of the history of an adnexal operation, its obstinacy to therapy and low-grade temperature. Gonococcus, complement fixation and cervical smear being negative, this diagnosis became less likely. The constant high level of the sedimentation rate throughout her stay is of marked interest.

CASE VI.—R. P., female, aged twenty-seven years, was admitted on the medical service, complaining of migratory joint pains for the past three weeks. Before admission she had developed generalized body pains which localized in the knees, ankles, wrists, shoulders and interphalangeal joints. These joints were involved at different times, but never showed signs of redness or swelling or limitation of motion. Physical examination negative except for a loud systolic murmur at the apex which is transmitted toward the axilla. P2 greater than A2. Joints are objectively negative. Electrocardiograph shows sinus tachycardia. Roentgen rays show joints negative; heart enlarged, with accentuation of right auricle, and left auricle and ventricle. Configuration is mitral.

Laboratory Data: Urine: specific gravity, 1020 to 1030; trace of albumin; occasional red blood cell; blood cultures, negative; Wassermann, negative; blood chemistry: glucose, 83 mg.; N.P.N., 30 mg.; total protein, 6.24; albumin, 4; globulin, 2.24; ratio, 1.7.

Blood counts: June 10.—R. 3.04, Hb. 58, W. 8,000, St. 8, S. 64, E. 1, Ly. 23, Mo. 4
June 12.—R. 2.95, Hb. 56, W. 10,400, St. 4, S. 57, E. 1, Ly. 35, Mo. 3
June 26.—R. 3.42, Hb. 58, W. 11,200, St. 5, S. 62, Ly. 28, Mo. 5
July 8.—R. 3.43, Hb. 60, W. 11,400, St. 6, S. 55, Ly. 37, Mo. 2

Sedimentation rates: June 13, 69%; June 26, 54%; July 2, 51%; July 8, 48%; July 14, 35%; July 22, 30%; July 29, 25%; August 4, 20.5%; August 11, 16%; August 19, 8%.

This case is one of acute rheumatic fever in which the joint manifestations played a minor rôle throughout the patient's illness. It was therefore sur-

prising to find that in spite of the lack of arthritic signs the sedimentation rate was very high, and although the entire illness seemed very mild, frequent blood tests showed the rate dropping very slowly though steadily. This case would tend to demonstrate that it is not the arthritis *per se* that causes the high sedimentation rate, and that the apparently mild case does not necessarily have a more rapid return to normal rates than those with numerous swollen and inflamed joints.

Case VII.—M. F., aged fifty-seven years, female, admitted with the chief complaints of pain over the sacral and lumbar region, over upper part of the sternum; swelling of the feet and loss of weight. Symptoms appeared insidiously about nine months ago with a localized sticking pain over the sacrum. A dull aching pain appeared over upper part of the sternum somewhat later. Swelling pain and redness of feet a week later. Patient has been bedridden during this illness and has lost 50 pounds. For the past few weeks the intensity of her joint pains has diminished. Pain is aggravated by any attempt to stand or walk. Physical examination reveals female markedly emaciated and apparently chronically ill. Musculature wasted and flabby. Both feet are red, swollen and tender to slight pressure. There is an area of exquisite tenderness over the upper end of the sternum. Pressure on ribs and over the pelvis elicits tenderness. Orthopedic consultation: lumbar spondylitis with arthritis of both ankles. Roentgen rays show senile atrophy of pelvis and lower lumbar vertebral structures with productive changes.

Laboratory Data: Urine: specific gravity between 1010 and 1030, no Bence-Jones protein, moderate white blood cells and epithelium; Wassermann, negative; blood chemistry, negative; blood count: R. 3.4, Hb. 59, W. 11,200, St. 2, S. 69, Ly. 22, Mo. 7, macrocytosis and microcytosis. Sedimentation rates: July 15, 69%; July 22, 70%; July 29, 69%; August 6, 69%.

This case is one of infectious arthritis with osteoarthritic changes. The arthritis deformans type usually involves the lumbar and sacroiliac joints, but may also involve others. Salicylates, physiotherapy and immobilization with plaster casts have been unable to influence or in any way help relieve the suffering of this patient. Sedimentation rate is high and will in all probability remain high. This type of arthritis coming on after the menopause is usually progressive and deforming.

Discussion. After having determined the amount of sedimentation present in various arthritic conditions, it was of interest to investigate whether the red blood cells dropped at varying rates in conditions caused by different etiologic agents. I therefore proceeded to record the amount of sedimentation every five minutes in a series of selected cases that had high sedimentation rates. In Table I we have 5 cases of divergent type.

Table I.—Graphic Representation of the Sedimentation Rate.

	0–5–10–15–20–25–30–35–40–45–50–55–60 (min.)
	%
1. Infectious arthritis (tuberculous)	0–25–65–77–80–81
2. Ca. of lung (multiple abscesses)	0–20–75–83–84
3. Ac. rheumatic fever, hyperpyrexia	0– 4–11–25–36–43–49–53–58–63–67–70–72
4. Uremia	0– 5– 9–15–21–26–35–45–58–66–73–74–77
5. Pulmonary tuberculosis	0– 7–13–21–28–33–37–41–45–48–50–52–54

In Table I the first case showed the maximal amount of sedimentation capable of being recorded, in twenty-five minutes. The height of the red cell column made further sedimentation impossible. In the second case there was flocculation of the entire cell column five minutes after introduction into the cylinder. Graph 1 shows nothing characteristic in the curves of either of the five curves.

CHART I.

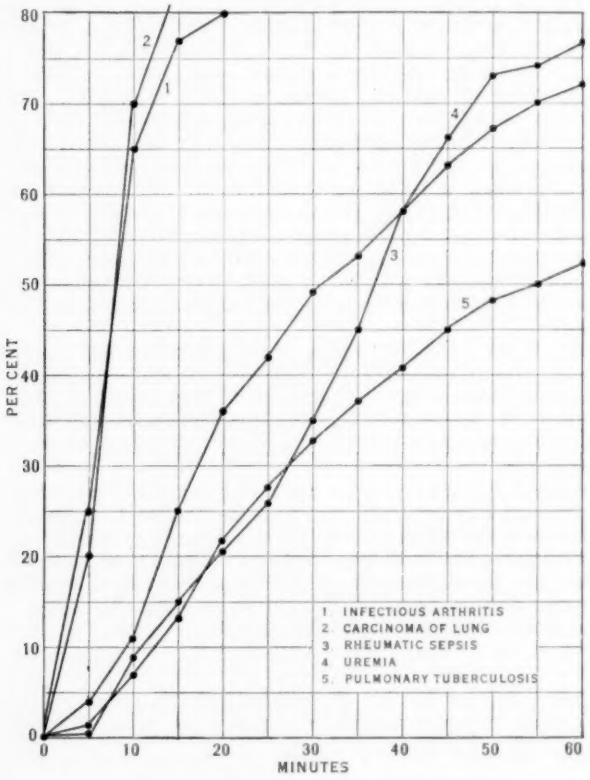


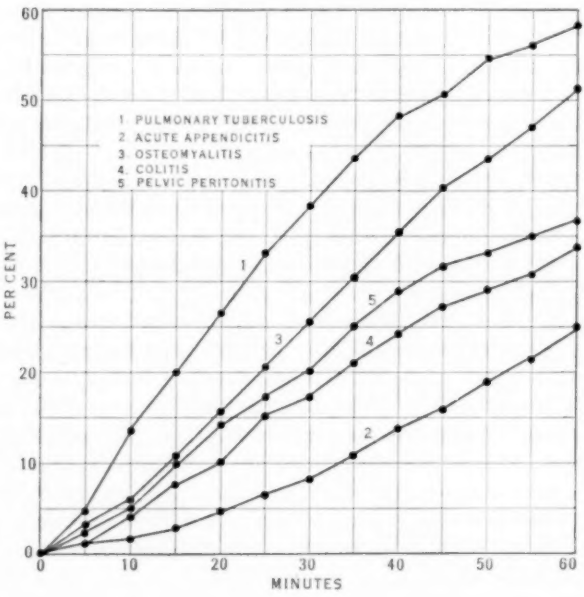
TABLE II.—GRAPHIC REPRESENTATION OF THE SEDIMENTATION RATE.

	0–5–10–15–20–25–30–35–40–45–50–55–60 (min.)
1. Pulmonary tuberculosis, nephritis	0–4–12–20–26–33–38–43–48–51–52–56–58 %
2. Acute gangrenous appendicitis	0–1– 2– 3– 4– 6– 8–10–13–15–19–22–25
3. Osteomyelitis	0–2– 5–10–15–20–25–30–35–40–45–48–51
4. Colitis	0–1– 4– 7–10–15–17–21–24–27–29–31–34
5. Pelvic peritonitis	0–2– 5–10–14–17–20–25–29–32–33–35–37

Table I and Graph 2 also show that the rate of sedimentation as recorded every five minutes is of no assistance inasmuch as there is nothing characteristic about any of the five curves.

Perusal of this entire group of cases showed the presence of slight to severe secondary anemias in the majority. Blood counts were not of outstanding importance, inasmuch as they showed as a rule a slight leukocytosis and occasionally a staff cell count as high as 9%. Eosinophils were usually present. Blood cultures were always sterile, and blood chemistry findings were not unusual except for the first case of tubercular arthritis with amyloidosis. Sedimentation tests, however, were of interest and of definite significance. Although the height of the sedimentation rate was not a differential point between the cases of acute rheumatic fever and those of secondary infectious arthritis, be it tuberculous, gonorrheal or focal,

CHART II.



the behavior of a series of tests, taken at frequent intervals, was very helpful. In cases of rheumatic fever I found a gradual drop of the sedimentation rate and return to normal, whereas in all the cases of infectious arthritis the sedimentation rate remained high. It was also of interest to find that very high rates were found in very mild cases. These rates were often as h gh as 60 to 70%. Furthermore we found that whereas the fever and symptoms of the patient with acute articular rheumatism disappeared as a rule three or four days after oral or rectal administration of large doses of salicylate, the sedimentation rate stayed high and did not return to normal until three to five weeks after the patient was free of all symptoms. The medical men observing these cases objected at

the beginning, because of the incompatibility of an apparently cured patient with a sedimentation rate that stayed high. We found, however, that this condition was the rule and advised that all the rheumatics be kept under observation as long as their sedimentation rates were high, even if their symptoms had disappeared. Meerovitch, on a basis of his study of 90 cases of rheumatic polyarthritis, feels that any patient released from treatment before the sedimentation rate has reached normal will come down with a recurrence in three weeks. He believes, however, that the amount of sedimentation is dependent largely on the acuteness of the disease. Ditges also believes that the amount of sedimentation runs parallel with the clinical manifestations. There are a few more points of interest: (1) What part does the anemia play in this reaction, and (2) do any of these cases of rheumatic polyarthritis become chronic? It is true that many of these cases have marked secondary anemias, and that their arthritic manifestations are trivial. And then again we also know that three or four days after institution of proper medication the symptoms all disappear but the sedimentation rate remains high. This point can be readily cleared up by taking sedimentation tests on a series of secondary anemia of the posthemorrhagic type, or even cases of pernicious anemia. I have found in this type of a series that the sedimentation rate rarely reached 15%. This can therefore never account for rates that often reach 70 or even 80%. Second, there still exists among the medical profession the term chronic rheumatism. This covers a vast number of ailments and symptoms such as muscle pains, joint pains without external local manifestations, and so forth. It was therefore of interest to see whether any of the cases in this group would show any tendency to become chronic. This was found not be be the case, as all of these cases gradually showed normal sedimentation rates of 3 to 5%. Upon return for observation these patients had normal rates and had no complaints to register. None of these cases had been discharged before the sedimentation rate had approached normal, taking no cognizance of their period of well-being. During the two years these cases have been under observation, I could find no recurrences or any tendency to chronicity.

As regards the cases of infectious arthritis, we can say that in spite of all types of therapy, salicylates, physiotherapy, vaccines, the sedimentation rates were high and showed no tendency to return to normal. Most of the cases were acute but tended to become chronic.

Last, I wish to say a few words concerning the sedimentation cylinder (Fig. 1). I have tried to utilize the best parts of both methods. I believe it is superior to the Linzenmeier method and its modifications as it is less time-consuming, more accurate and

practical. By this method it is very simple to do a dozen tests and then make the readings forty-five minutes later. To prove this to myself I used both methods on the same specimens of blood for a period of three months. I found during this period that it was utterly impossible to do anything but watch the Linzenmeier tubes, whereas one could go about the hospital taking care of other matters and return in three-quarters of an hour to record the readings on the cylinder. I also found that whereas the high sedimentation rates checked well with those cases that came down in less than thirty minutes, there were marked discrepancies in those taking more than an hour. Its advantage over the Fahraeus was that the tube was calibrated and could be read off in per cents; no complicated stand and spring were necessary; and last, that it had an inner diameter of 5 mm. and did away with the possibility of capillary attraction and rubbing between the red cells and the walls of the tube.

Summary. One hundred and fifty cases of rheumatic fever and 25 cases of infectious arthritis were observed and the following points noted:

1. The sedimentation rate was high in rheumatic fever and did not return to normal with the disappearance of the arthritic symptoms. The return to normal of 3 or 5% did not occur until three to seven weeks after the disappearance of complaints.

2. Severity of the joint manifestations was not accompanied by a proportionately high sedimentation rate.

3. Sedimentation rate did not return to normal any faster in mild cases than in the more severe.

4. As far as the sedimentation rate gives evidence, cases of acute articular rheumatism do not tend to become chronic.

5. Cases of acute rheumatic fever are not to be discharged before the sedimentation rate reaches normal.

6. The sedimentation in these cases is not due to the amount of anemia that is always present.

7. The sedimentation rate in cases of infectious arthritis is very high (60 to 80%) and usually does not return to normal, unless the cause can be discovered and removed.

8. This procedure does not differentiate the various types of secondary arthritis such as tuberculous, gonorrheal or acute arthritis deformans.

9. The high sedimentation rate is not due to the anemia that is usually present.

This procedure is of no diagnostic value in arthritis, but is of great help in prognosis and an essential guide in treatment and convalescence. No rheumatic fever should be discharged from close observation until the sedimentation rate has reached normal. Any case that simulates acute rheumatic fever but which shows no tendency

for the sedimentation rate to gradually return to normal can be understood to be one of secondary arthritis.

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UROBILINURIA IN CHILDREN WITH RHEUMATIC HEART DISEASE.

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Recent studies by Elman and McMaster[1] on the physiology and pathology of urobilin have given us new facts concerning the formation and excretion of this substance. Urobilin is formed in the intestines from the bile pigment, bilirubin, by a reduction process associated with certain bacteria. Urobilinogen, the chromogen of urobilin, is probably first formed and excreted as such. It is, however, readily oxidized to the pigment, urobilin, when exposed to light. The method used in our study for determining urobilin was that of Elman and McMaster. During the experimental procedures, urobilinogen is converted into urobilin. The term, urobilin, as employed in this report includes therefore, all the reduction products of the bile pigment, bilirubin.

It has been shown that urobilin is formed only when bile actually

enters the intestines. A large part of the urobilin is excreted in the feces. A certain part, however, is absorbed from the intestines by the portal circulation and carried to the liver where it may be removed from the blood. Normally the liver is able to remove all or nearly all of the urobilin carried to it by the portal circulation, so that very little or none reaches the systemic circulation to be excreted in the urine. In certain hepatic conditions, the ability of the liver to remove this substance from the blood may be interfered with, and a urobilinuria results. An excess of urinary urobilin has been reported principally in the clinical conditions associated with excessive destruction of erythrocytes, and those causing injury to the liver cells. Examples of these are: pernicious anemia; periods following blood transfusions; cirrhosis; acute yellow atrophy; liver degeneration due to infectious diseases, such as malaria, pneumonia, scarlet fever, typhoid fever, and rheumatic fever; and passive congestion due to heart failure. A urobilinuria has also been observed in apparently healthy individuals.

It is generally agreed that small amounts of urobilin may be present in the urine in normal subjects. It has not been definitely established what constitutes a normal or an abnormal amount excreted in a twenty-four-hour period. This fact must be borne in mind when we interpret our experimental results, and should also make us cautious when we are tempted to assign clinical significance to small increases in this constituent during pathologic states. Frederick Müller reports as high as 20 mg. per twenty-four-hour period; Hoppe-Seyler from 80 to 140 mg.; and Saillet from 30 to 130 mg.[2] It has been pointed out that these variations probably were due to the fact that different methods had been employed and that sources of error existed in the analytic procedures. Edelman,[3] employing the method of Elman and McMaster, observed a urobilinuria at different times in normal children. He considers 3 mg. per 100 cc. or 30 mg. per 1000 cc. as the upper normal limit. However, the expression of urobilin excretion in terms of concentration cannot be considered a satisfactory one, since the total urobilin output in a twenty-four-hour period is necessarily dependent on the volume of urine excreted in the same period. An estimation of 3 mg. per 100 cc. on a 1000-cc. volume of urine would mean a total excretion of 30 mg., but if the volume were 2000 cc. the total excretion would be twice that amount or 60 mg. It would seem then that an excretion of 60 mg. in twenty-four hours need not necessarily indicate a serious pathologic condition.

Marked increases in the urinary urobilin excretion during cardiac decompensation have been observed by various investigators.[3,4,5,6,7] Recently Edelman[3] reported observations on a large number of children. These cases were divided into 4 groups: A control group composed of normal children, a comparative group composed of children confined to bed with an illness other than

heart disease, a group of ambulatory heart cases, and a group of children with decompensated hearts. Of his control group, 4% were positive, of the comparative group, 34%, of the ambulatory group, 26%, and of the decompensated group, 88%. As a result of his observations, Edelman asserts that the urinary urobilin estimations may serve the clinician as an indicator of the progress of the affected heart, and that this test is more sensitive and reliable than any of the other standards.

Our study was concerned with the urinary urobilin estimations on children with rheumatic heart disease during different stages of the disease. Determinations were made on 57 ambulatory cases, 4 children with recurrent rheumatic carditis without congestive failure, and 10 cases with congestive heart failure, Class III cases. The ambulatory cases were divided as follows: 1, Class I; 33, Class IIA; 21, Class IIB; 1, Class IV, and 1, Class V. The Class III children represented different degrees of congestive heart failure.

In the Class IIA cases, the figures ranged from 0 to 84 mg. The average total output in twenty-four hours is 15 mg. If the estimation is expressed in milligrams per 100 cc., no child had more than 3 mg. In the IIB cases the figures were slightly higher, ranging from 0 to 102.6 mg. The average total output in twenty-four hours is 26.5 mg. Six children presented values over 3 mg. per 100 cc. However, in only 3 of these was the total output per twenty-four hours above 60 mg., and at subsequent examinations considerably lower values were obtained. Of the 4 children with recurrent rheumatic carditis, but with no signs of congestive failure, 3 showed values ranging between 0 and 38 mg. per twenty-four hours. One child had an output of 12 mg. per 100 cc. at one examination. One week later 3 mg. per 100 cc. were obtained. The results observed in the Class III children are presented in the report of the cases. These observations indicate that the highest urinary urobilin values were noted in the cases with congestive failure.

Comment. Although the highest urobilin figures were obtained in children with congestive heart failure, a study of these patients over a period of time revealed the fact that congestive failure was not always accompanied by abnormal urobilin values; or as noted in some of the ambulatory children, an increased urinary urobilin output was not necessarily associated with congestive failure. In the IIA cases the total urobilin excretion per twenty-four hours was less than 50 mg. with the exception of 1 case which showed a value of 84 mg. A number of these children presented negative values. The child with 84 mg. showed a figure of 19.5 mg. at a subsequent examination. Four of the IIB cases showed figures above 50 mg. per twenty-four-hour period. All of these children presented lower values at a second examination. The average total output of the IIB cases is 26.5 mg. as compared to 15 mg. for the IIA cases.

If one compares the output of the individual cases in each group, however, not a very appreciable difference is noted. The urinary urobilin estimations apparently are of no additional aid in classifying ambulatory children with heart disease.

Three of the 4 children with recurrent rheumatic carditis, but with no clinical evidence of congestive failure, showed no increase in the urinary urobilin. One child apparently presented slightly elevated figures for several days, but in this case we failed to express the results in total output per twenty-four hours.

From an analysis of our Class III children, we found that an increased urinary urobilin excretion may occur during congestive heart failure. This fact has been demonstrated by a number of investigators. Our interest in urobilinuria in heart disease was concerned with the clinical value, and to determine whether or not a close relation existed between the degree of urobilinuria and the efficiency of the heart. Since passive congestion and edema of the liver of varying degree often occurs during congestive heart failure, and a urobilinuria frequently results, it was suggested that urinary urobilin estimations might serve as a guide in determining the cardiac efficiency. We were unable to substantiate this viewpoint. In general, the highest figures were observed during marked congestive failure. However, great variations occurred from day to day. With an increase in the severity of the signs and symptoms of failure, an increase of urinary urobilin output was not always observed. In some cases in early congestive failure, the urobilin excretion was well within normal limits, or not any higher than in patients with no heart disease, or in patients with organic heart disease but with no evidence of congestive failure. In some instances the urobilin had reached the normal level when there was still evidence of some congestive failure, or when it was considered inadvisable to allow the patient to be up and about. In Case I the onset of failure was sudden, and was accompanied by a temperature of 100.4° F. (rectal) which indicated a recurrent rheumatic infection. The urobilin estimation on a single urine specimen was only 4 mg. per 100 cc. An estimation on a twenty-four-hour specimen of urine could not be performed until a day later. It will be noted that the twenty-four-hour urobilin output was only slightly increased and not any higher than may be observed in the absence of congestive heart failure. Urobilin determinations were made at weekly intervals in this case until December 11, 1929, and then daily until the patient's death. During all this time the patient was considered a Class III case, and although variations in the clinical condition were noted, there was always some clinical evidence of congestive failure present. The urobilin output also varied considerably, but was often within the normal range. The interesting point in this case is the fact that during the last ten days of the

patient's life, the urobilin excretion decreased and was well within normal limits while the signs and symptoms of heart failure became exaggerated. Jaundice became very deep and edema and body weight increased markedly. The liver was 10 cm. below the costal margin. Case II developed a recurrent attack of rheumatic fever. In this case urobilin estimations were made before there were clinical signs of failure. These estimations were all negative. On March 20, dyspnea was noted, and the liver was palpable and tender, indicating beginning congestive failure. The urobilin was still negative. The congestive failure became progressively worse, basal râles and edema appeared, and the liver increased in size. The urobilin output, however, never increased above the normal value. Case III was a child with rheumatic heart disease and congestive failure. He was always a Class III case while under observation. Marked variations in urobilin excretion were observed, some of the figures being well within normal limits. During January and February, 1930, daily urobilin estimations were negative or well within normal limits, although signs and symptoms of congestive failure, such as edema, basal râles, enlarged and tender liver, and decreased urinary output were constantly present. Case IV is another child with congestive failure during the entire period of observation to the time of death. Only a trace of urobilin was observed during the first four days of observation. Later determinations showed definite variations, although normal values were often obtained. There was no indication of an increase in urobilin output just before death. The results obtained in the other cases are shown in the report of the individual cases.

Report of Ten Cases.—Case I.—A boy, aged sixteen years, with rheumatic heart disease, mitral insufficiency and stenosis developed acute heart failure on July 15, 1929. He complained of nausea and vomited. The temperature was 100.4° F. The liver was three finger breadths below the costal margin. Basal râles were present. There was slight edema of the ankles. The urobilin was 4 mg. per 100 on a single urine specimen. A determination on a twenty-four-hour specimen could not be made until the morning of the seventeenth. The value was 76.2 mg. On August 11, the urobilin was 23.2 mg. but there was still evidence of congestive failure as evidenced by an enlarged and tender liver. The urobilin values varied a great deal from day to day. The highest figure obtained was 340.8 mg., the lowest 0. Since the onset of the congestive failure to the time of death on February 1, 1930, the patient was always considered a Class III case. During the last week of life congestive failure was marked. The urobilin was consistently low, ranging between 12.3 and 46 mg. per twenty-four-hour period.

Case II.—A girl, aged twelve years, was admitted with a diagnosis of rheumatic heart disease, mitral insufficiency and stenosis. Symptoms of a recurrent attack of rheumatic fever were noted on March 3, 1930. Signs of congestive heart failure were observed March 20. Urobilin estimations on twenty-four-hour urine specimens were negative from March 14 to 22,

two days after congestive failure was present. The urobilin values were 27 mg. on March 23, 20 mg. the following day, and 12 mg. March 25. Congestive failure was of a moderate degree during this time.

CASE III.—A boy, aged eleven years, with a diagnosis of rheumatic heart disease, mitral insufficiency and stenosis, and aortic insufficiency developed a congestive failure on March 14, 1929. The child was always considered a Class III case since the onset of failure. The urobilin figures varied from 288 mg. to 7.5 mg. per twenty-four hours. The child was discharged in November, 1929, but was readmitted in January, 1930, with signs and symptoms of congestive failure. Since the readmission, urobilin estimations were often negative, and never over 40 mg. during a twenty-four-hour period. Varying degrees of congestive failure were present at the time the determinations were made.

CASE IV.—A boy, aged nine years, was admitted on July 15, 1929, with a diagnosis of rheumatic heart disease, mitral stenosis and insufficiency, and congestive failure. He was always a Class III case until he died on February 9, 1930. Urobilin estimations showed only a trace on the first four days following his admission. The majority of the urobilin values were well within normal limits, only six being above 50 mg.

CASE V.—A girl, aged sixteen years, with rheumatic heart disease, mitral stenosis and insufficiency and aortic insufficiency, developed a recurrent carditis and auricular fibrillation. On October 25 signs and symptoms of congestive failure were noted. The urobilin was 326.4 mg. on October 27. On the twenty-ninth it had dropped to 45.9 mg. and the following day was 34.2 mg. The temperature was 100.2° F., there were moist râles over both bases of the lungs, and dyspnea was present at rest. With the aid of digitalis (1 cat unit a day) the clinical condition improved to such an extent that the child was able to be up and about without experiencing any discomfort. Daily urobilin determinations were made while the child was ambulatory. The figures varied from time to time between 0 and 60 mg. No signs or symptoms of congestive failure were evident during this time. For a period of two weeks the child was kept in bed to see whether or not rest would have any effect on the urobilin values, however, no difference was noted between the urobilin excretion during the period of rest and the periods of slight physical activity in this case.

CASE VI.—A girl, aged thirteen years, was admitted with a diagnosis of rheumatic heart disease, mitral insufficiency and stenosis, recurrent carditis, and congestive failure. The urobilin estimation was 204 mg. About a week later all signs of failure had disappeared and normal values for the urobilin were obtained.

CASE VII.—A boy, aged sixteen years, developed a recurrent carditis and congestive failure on December 24, 1929. The urobilin output was 103.2 mg. Eleven days later it was 348 mg. On January 6 the urobilin was negative and from that date on, remained with normal limits. Signs and symptoms of congestive failure disappeared at this time.

CASE VIII.—A girl, aged sixteen years, was admitted with a diagnosis of rheumatic heart disease, mitral insufficiency and stenosis, and auricular fibrillation. On June 15, 1929, signs and symptoms of congestive failure

were noticed (dyspnea, nausea, vomiting, enlarged and tender liver, basal râles). The urobilin output during the following day was 60.6 mg., two days later 24 mg. Daily determinations since that date showed only small amounts of urobilin excretion.

CASE IX.—A girl, aged sixteen years, diagnosed as rheumatic heart disease, mitral insufficiency and stenosis, and auricular flutter began to complain of anorexia and slight cough on July 1, 1929. The symptoms gradually increased in severity. On July 9, vomiting became a prominent symptom. The rate at the apex was 108. The liver was slightly enlarged and tender. On July 1, the urobilin output was only 12.6 mg. and on the ninth, 3.2 mg. The patient was digitalized on July 12, and was much improved two days later. Her progress was rapid and in two weeks was able to be up and about.

CASE X.—A boy, aged eight years with rheumatic heart disease, mitral insufficiency and stenosis, and auricular fibrillation. He developed a mild congestive failure after digitalis had been discontinued. The highest urobilin output during this time was 73.8 mg.

Summary. The urinary urobilin estimations are of no help in classifying IIA or IIB cases of heart disease. Children with a recurrent infection of the heart, but with no evidence of congestive failure may show normal values for the urobilin excretion in a twenty-four-hour period. High values for the urinary urobilin may be observed in children with congestive heart failure, but a high urobilinuria is not necessarily present in these cases, nor does a hyperurobilinuria in children with rheumatic heart disease always mean congestive failure. The urobilinuria does not bear a consistent relationship to the degree of congestive failure, and, therefore, cannot be considered a reliable index of the functional efficiency of the heart. It is of no significant value in the diagnosis of the degree of damage, prognosis, or the management of the cardiac child.

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THE EFFECT OF IRRADIATED ERGOSTEROL ON THE COMPOSITION OF GASTRIC AND PANCREATIC JUICES.*

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During the course of studies[1, 2] concerning the effect of irradiated ergosterol on the calcium and phosphorus metabolism of adults we observed an increased retention of both of these salts. These studies, however, did not enable us to state conclusively the exact mode of action of this vitamin D preparation.

We had thought that the increased retention of calcium and phosphorus might be due to more complete absorption of these salts from the gastrointestinal tract, but had no proof as to the *modus operandi*. Certain observations on one of our former patients, as well as the work of other investigators,[3, 4, 5, 6, 7, 8] directed our attention to the study of composition of gastric and pancreatic juices before and after such vitamin therapy.

For instance, this patient (Mr. R. L., Case I[2]) noted a tendency to anorexia and diarrhea after he had received 30 mg. of irradiated ergosterol a day for twelve days. The stools resembled those seen in the fatty diarrhea associated with pancreatic disease. Although these symptoms disappeared before the dose of irradiated ergosterol was reduced, we wondered if they indicated a disturbance of pancreatic function. Two duodenal analyses at this time revealed normal proteolytic, amylolytic and lipolytic enzyme activity. Evidently the fatty stools were not due to demonstrable depression of the lipolytic enzyme activity. Two gastric analyses (ergamin acid phosphate was given at the time of the test meal in each case) revealed a very low gastric acidity. (See table below and Curves I and II of Chart I.) We had not determined his gastric acidity before the irradiated ergosterol therapy and therefore did not know

* We wish to take this means of thanking the Winthrop Chemical Company for the irradiated ergosterol used in these experiments.

whether this low gastric acidity was caused by its administration or represented a preëxisting abnormal gastric secretion. It did, however, seem worthy of further study; therefore, he was sent home for eighty-one days and later observed (*v. infra.*, Case I).

TABLE I.—GASTRIC ANALYSES DURING THE ADMINISTRATION OF IRRADIATED ERGOSTEROL.

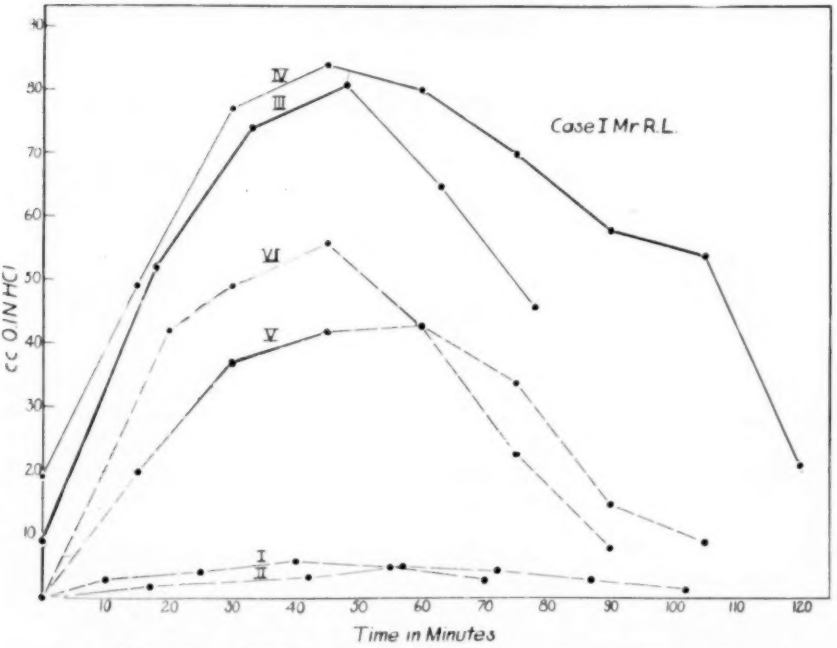
Case I.	Date.	Time.	Vol., cc.	Free HCl, cc. 0.1 N per 100 cc.	Total acidity, cc. 0.1 N per 100 cc.	Chlorids, cc. 0.1 N per 100 cc.	Remarks.
Mr. R. L.	Jan. 23	Fasting	94	0.30	0.60	104.0	Received 30 mg. irradiated ergosterol from Dec. 8 to Jan. 4; 15 mg. a day from Jan. 4 to 26.
See:		10 min.	94	3.10	4.80	116.5	
Chart I		25 "	88	4.60	5.90	125.0	
Curve I		40 "	50	5.80	6.50	127.5	
		55 "	29	4.80	5.00	122.5	
		70 "	3	3.10	4.40	N.S.Q.	
Mr. R. L.	Jan. 25	Fasting	30	...	1.14	121.5	Two days later; same dosage (15 mg. per day), of irradiated ergosterol.
See:		2 min.	94	0.10	0.42	102.5	
Chart I		17 "	110	1.72	2.38	116.5	
Curve II		42 "	90	3.75	4.44	117.5	
		57 "	34	5.26	6.50	132.5	
		72 "	8	4.80	6.44	125.0	
		87 "	5	2.92	4.90	117.5	
		102 "	5	1.16	2.78	117.5	

Besides such suggestive evidence, there are many data in the literature which indicate that vitamin D therapy in some manner affects the reaction of the intestinal tract. Other workers[3] have observed that the intestinal contents in rickets are abnormally alkaline. As improvement takes place under vitamin D treatment, the intestinal contents become acid. Could this increased acidity of the intestinal contents be the result of changes in the composition of either the gastric or pancreatic juice? The finding of a lower gastric acidity in rickets would lend support to such a hypothesis.[5] Certainly any increase in the acidity of the gastrointestinal tract would favor more complete absorption of calcium.[6, 8]

The Composition of Gastric and Pancreatic Juice Before and After Irradiated Ergosterol Therapy in Patients. In order to observe whether or not the administration of irradiated ergosterol had any effect on the composition of gastric or pancreatic juices, the following tests were performed. Irradiated ergosterol was administered to 4 adults. In 3 of these subjects (apparently normal) the gastric juice was analyzed before and after irradiated ergosterol administration. The duodenal contents were tested for pancreatic enzyme activity before and after this therapy. (Case III, Miss L. D., had no tests made on the duodenal contents before the administration of irradiated ergosterol was instituted.) Only gastric analyses were made on the patient with osteoporosis (Case IV, Mrs. M. B.).

Methods. The procedure used in analyzing the gastric juice was as follows: The patient was not allowed breakfast. A small tube was passed to the stomach through the nose and the fasting contents aspirated. Then a test meal of 100 cc. of 7% alcohol was given through the tube; in all cases 1 cc. (0.5 mg.) of ergamin acid phosphate was administered intramuscularly at the same time. Samples were collected at ten to fifteen minute intervals; the volume was measured at each withdrawal and all but 10 cc. returned to the

CHART I.—SHOWING THE EFFECT OF IRRADIATED ERGOSTEROL ON THE SECRETION OF FREE HYDROCHLORIC ACID.



Curve I shows the values obtained after irradiated ergosterol had been administered forty-six days. Thirty milligrams were given each day for the first twenty-six days and 15 mg. a day the last twenty days. Curve II represents the values obtained on the forty-eighth day of this period of study. Curves III and IV represent the normal free hydrochloric acid secretion in this patient. Curve V represents the values obtained after the administration of 5 mg. a day for twenty-five days. Curve VI represents the values obtained on the twenty-sixth day (dose the same, 5 mg. a day).

stomach. This was continued until the volume obtained at an aspiration became too small to make an analysis (less than 5 cc.). Each collection of juice was titrated against $\frac{N}{10}$ sodium hydroxid in the usual manner. Töpfer's solution and phenolphthalein were used as indicators in order to determine the amount of free hydrochloric and combined acid present. The chlorid content of each sample was determined by the method of Fiske.[9] The presence or absence of bile, mucus and blood was noted.

The procedure used in analyzing the duodenal contents was as follows: The patient was not allowed breakfast. A tube was passed to the duodenum and its position checked by fluoroscopy. Then 2 ounces of 40% cream were given through the tube and collection of duodenal contents begun. The first portion obtained was mixed with cream; accordingly all material was discarded until a clear fluid began to flow. About 50 cc. of the clear duodenal contents were then collected for analysis. The activity of the pancreatic enzymes was determined according to the method outlined by McClure and others.[10, 15]

TABLE II.—GASTRIC ANALYSES BEFORE AND AFTER THE ADMINISTRATION OF IRRADIATED ERGOSTEROL.*

Case.	Date.	Time.	Vol., cc.	Free HCl, cc. 0.1 N per 100 cc.	Total acidity, cc. 0.1 N per 100 cc.	Chlorids, cc. 0.1 N per 100 cc.	Remarks.
Mr. R. L.	April 16	Fasting	?	9	15	41.5	Seventy-five days since administration of irradiated ergosterol.
See:		18 min.	75	52	61	67.5	
Curve III		33 "	62	74	86	89.0	
Chart I		48 "	58	81	93	96.0	
		63 "	6	65	83	94.0	
		78 "	1	46	60		
Mr. R. L.	April 22	Fasting	44	19	38	105.0	Eighty-one days without irradiated ergosterol.
See:		15 min.	83	49	50	62.5	
Curve IV		30 "	107	77	84	65.0	
Chart I		45 "	70	84	95	107.5	
		60 "	54	80	97	103.5	
		75 "	50	70	84	93.5	
		90 "	28	58	76	88.5	
		105 "	13	54	65	81.0	
		120 "	12	21	36		
Mr. R. L.	May 25	Fasting	..	0	8	79.0	After 25 days on 5 mg. irradiated ergosterol a day.
See:		15 min.	140	20	29	24.5	
Curve V		30 "	140	37	46	65.0	
Chart I		45 "	106	42	53	70.0	
		60 "	73	43	54	74.0	
		75 "	42	34	52	75.0	
		90 "	2	15	26	55.5	
		105 "	1	9	21		
Mr. R. L.	May 27	Fasting	..	0	14	67.6	Two days later on same therapy.
See:		20 min.	63	42	54	71.6	
Curve VI		30 "	64	49	62	74.0	
Chart I		45 "	55	56	70	87.5	
		60 "	45	43	58	84.5	
		75 "	18	23	36	72.0	
		90 "	4	8	29	70.5	

* Second period of study on Case I, Mr. R. L. The first two analyses were obtained before irradiated ergosterol was given a second time. The last two analyses were made after he had received 5 mg. a day for twenty-five and twenty-seven days, respectively.

Case Reports.—CASE I. Mr. R. L., a student, aged nineteen years, returned to the metabolism ward for a second period of observation after an interval of eighty-one days without irradiated ergosterol therapy. Gastric analyses performed on the seventy-fifth and eighty-first days after cessation of the first vitamin D medication showed a normal gastric acidity on both occasions. (See Curves III and IV of Chart I, and Table II.) These results are quite striking when compared to the extremely low gastric acidity which had been observed after this same patient had received 30 mg. of irradiated ergosterol per day for almost seven weeks. (Results of this first period of study are shown in Table I, and in Curves I and II of Chart I.)

During the second period of study he received only 5 mg. of irradiated ergosterol each day (April 30 to June 1, 1929). Gastric analyses made on the twenty-fifth and twenty-seventh days after instituting this therapy showed a definite reduction of the gastric acidity. However, the reduction in acidity was not so marked as had been observed during the first period of study. (See Table II, and Curves V and VI of Chart I.) Duodenal analyses done during the three different experimental periods: (I. While receiving 30 mg. of ergosterol a day. II. The control period. III. During the administration of 5 mg. per day) showed no appreciable changes in the activity of the pancreatic ferments except a slight depression of activity of the amylolytic enzyme in Period I. (See Table III.)

TABLE III.—PANCREATIC ENZYME ACTIVITY BEFORE AND AFTER IRRADIATED ERGOSTEROL THERAPY.

Case. I.	Date, 1929.	Pancreatic enzyme.			Irradiated ergosterol, mg. per day.
		Proteolytic.*	Lipolytic.†	Amylolytic.‡	
Mr. R. L.	Jan. 26	0.15	1.05	0.12	30 mg. from Dec. 8 to Jan. 4; 15 mg. from Jan. 4 to 26.
	30	5.80	1.75	0.25	Same dose (15 mg. a day).
	April 29	5.43	...	2.12	No ergosterol for 79 days.
	30	2.28	0.50	1.44	No ergosterol for 90 days.
	May 3	...	1.47	...	15 mg. from April 30 to May 3.
	28	4.87	1.78	3.21	5 mg. from May 3 to 28.
	29	5.58	2.80	4.40	5 mg.

* Figures represent the milligrams of nonprotein nitrogen developed from 9 cc. of a 0.5% solution of casein by 1 cc. of diluted (1 to 50) duodenal contents.

† Figures represent the acidity developed by 1 cc. of diluted (1 to 50) duodenal contents from 9 cc. of cottonseed-oil emulsion as expressed in cubic centimeters of $\frac{N}{10}$ sodium hydroxid used in titration.

‡ Figures represent milligrams of sugar developed from 9 cc. of a 4% solution of soluble starch by 1 cc. of diluted (1 to 50) duodenal contents.

For details of method see paper by McClure and others.[10]

Lower Limit of Normal Pancreatic Enzyme Activity Values.

Proteolytic.	Lipolytic.	Amylolytic.	As determined by:
1.46	0.90	0.75	McClure, *et al.*[10]
1.50	0.75	0.75	Jones, *et al.*[15]

Any values lower than those given above should be considered as abnormal. Any values higher should be considered normal.

CASE II.—Mr. D. C., a medical student, aged twenty-five years, volunteered for a similar period of study. Two gastric analyses were done before the therapy was started. From Table IV and Curves I and II of Chart II one notes he had a normal gastric acidity. He received 5 mg. irradiated ergosterol from April 29 to May 21, 1929 (twenty-two days). The dose was then increased to 10 mg. a day and continued until June 15, 1929 (twenty-five days longer). Therefore, this vitamin D preparation was given daily for forty-seven days. About May 15 he began to have two bowel movements a day. By the last of May this had increased to three or four a day. All stools were soft and well formed. At no time did he develop a true diarrhea

or complain of gaseous distention or any other untoward symptoms. Gastric analyses performed on May 21 and June 13 are shown in Table IV and in Curves III and IV of Chart II. The average of these two curves is lower than the average of those before medication was started, but not so great a reduction as was observed in Case I.

TABLE IV.—GASTRIC ANALYSES BEFORE AND AFTER IRRADIATED ERGOSTEROL ADMINISTRATION.

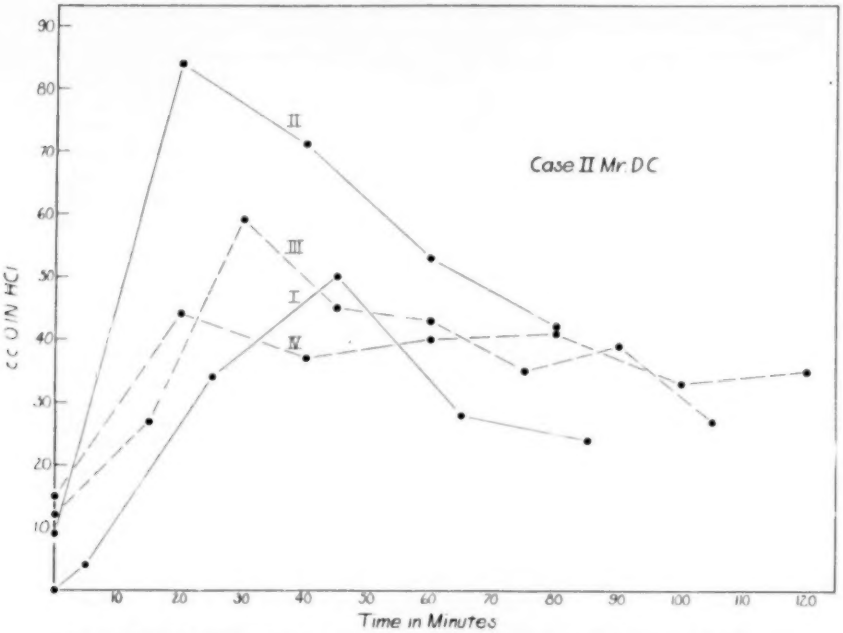
Case II.	Date.	Time.	Vol., cc.	Free HCl, cc. 0.1 N per 100 cc.	Total acidity, cc. 0.1 N per 100 cc.	Chlorids, cc. 0.1 N per 100 cc.	Remarks.
Mr. D. C.	Mar. 23	Fasting	0	0	6	57.5	Before therapy.
See:		5 min.	130	4	8	23.0	
Chart II		25 "	98	34	48	63.5	
Curve I		45 "	93	50	62	75.0	
		65 "	70	28	38	72.5	
		85 "	33	24	38	72.5	
Mr. D. C.	April 20	Fasting	0	9	22	88.5	Before therapy.
See:		20 min.	48	84	96	115.0	
Chart II		40 "	33	71	85	106.0	
Curve II		60 "	18	53	63	91.0	
		80 "	15	42	56	83.5	
Mr. D. C.	May 21	Fasting	..	12	20	89.5	After 21 days of irradiated ergosterol therapy.
See:		15 min.	..	27	38	50.5	
Chart II		30 "	37	59	73	96.5	
Curve III		45 "	36	45	57	93.5	
		60 "	46	43	58	93.0	
		75 "	23	35	52	87.0	
		90 "	25	39	63	90.5	
		105 "	12	27	45	93.0	
Mr. D. C.	June 13	Fasting	50	15	31	86.0	After 44 days ergosterol therapy.
See:		20 min.	51	44	60	77.0	
Chart II		40 "	47	37	55	94.5	
Curve IV		60 "	72	40	60	99.0	
		80 "	70	41	58	83.5	
		100 "	29	43	61	106.0	
		120 "	20	35	55	103.5	

The 3 duodenal analyses before medication was given checked each other surprisingly well. Two duodenal analyses while on irradiated ergosterol showed a definite depression of the activity of all 3 pancreatic enzymes when compared to the values obtained during the premedication period. (See Table V.) Although the values obtained during the administration of irradiated ergosterol are within the normal limits for such determinations,[10, 15] (see footnote, Table III), the fact that they are considerably lower than the control values obtained in this case would seem to be significant. We feel justified in considering this a depression of pancreatic enzyme activity as a result of irradiated ergosterol administration.

TABLE V.—PANCREATIC ENZYME ACTIVITY BEFORE AND AFTER IRRADIATED ERGOSTEROL THERAPY.

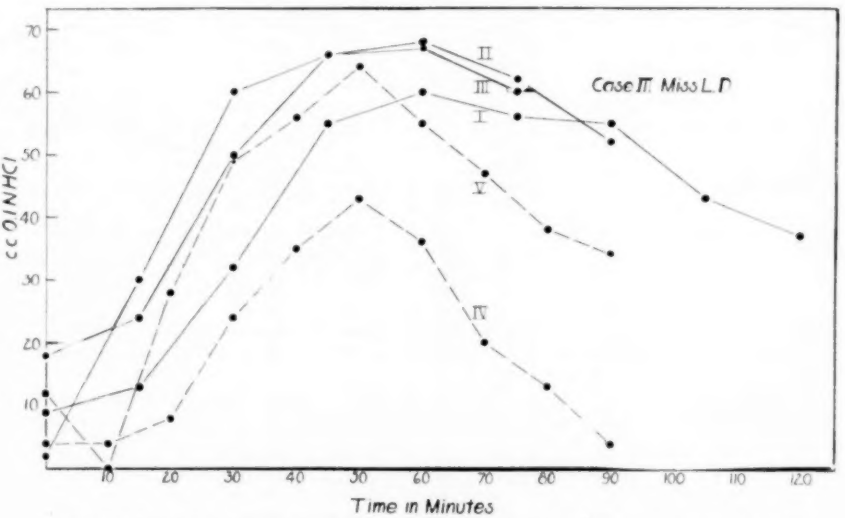
Case II.	Date, 1929.	Pancreatic enzyme.			Irradiated ergosterol dosage.
		Proteolytic.	Lipolytic.	Amylolytic.	
Mr. D. C.	Mar. 13	4.95	1.78	3.53	Before therapy started.
	16	4.57	1.70	...	Before therapy started.
	19	4.75	1.75	5.78	Before therapy started.
	May 23	2.90	1.28	2.42	5 mg. a day for 22 days.
	June 29	1.72	1.24	1.17	After 46 days of therapy.

CHART II.—SHOWING THE EFFECT OF IRRADIATED ERGOSTEROL ADMINISTRATION ON THE SECRETION OF FREE HYDROCHLORIC ACID.



Curves I and II represent the values obtained before therapy was started. Curves III and IV represent the values presented in Table IV. Curve III shows the values obtained following the daily administration of 5 mg. a day for twenty-two days. Curve IV represents values after forty-four days of therapy. The first twenty-two days the dose was 5 mg. a day; the last twenty-five days it was 10 mg. a day.

CHART III.—SHOWING THE EFFECT OF IRRADIATED ERGOSTEROL ADMINISTRATION ON THE SECRETION OF FREE HYDROCHLORIC ACID.



Curves I, II and III represent the values obtained before therapy was started. Curve IV represents the values obtained after one hundred and forty days of this medication (10 mg. a day). Curve V was obtained on the one hundred and forty-second day (dosage unchanged).

CASE III.—Miss L. D., a student nurse aged twenty-one years, was given 10 mg. of irradiated ergosterol per day fom May 28 to October 19, 1929 (one hundred and forty-two days). From Table VI and Chart III it is noted that the gastric acidity was slightly but definitely reduced after one hundred and forty days on irradiated ergosterol. No determinations of pancreatic ferment activity were made before medication was started. The one done at the end of the experiment was well within normal limits (See Table VII).

TABLE VI.—GASTRIC ANALYSES BEFORE AND AFTER THE ADMINISTRATION OF IRRADIATED ERGOSTEROL.

Case III.	Date.	Time.	Vol., cc.	Free HCl, cc. 0.1 N per 100 cc.	Total acidity, cc. 0.1 N per 100 cc.	Chlorids, cc. 0.1 N per 100 cc.	Remarks.
Miss L. D.	May 16	Fasting	..	9.0	22.0	98.5	Before therapy.
See:		15 min.	87	13.0	21.0	34.0	
Curve I		30 "	88	32.0	39.0	56.0	
Chart III		45 "	90	55.0	63.0	79.5	
		60 "	73	60.0	70.0	86.5	
		75 "	60	56.0	67.0	89.0	
		90 "	23	55.0	70.0	90.5	
		105 "	21	43.0	58.0	88.0	
		120 "	10	37.0	54.0	89.5	
Miss L. D.	May 25	Fasting	10	18.0	39.0	87.0	Before therapy.
See:		15 min.	40	24.0	34.0	55.5	
Curve II		30 "	70	50.0	62.0	82.5	
Chart III		45 "	82	66.0	83.0	98.0	
		60 "	72	68.0	82.0	99.5	
		75 "	33	62.0	75.0	84.0	
		90 "	1	52.0	67.0		
Miss L. D.	May 27	Fasting	..	2.0	18.0	96.5	Before therapy.
See:		15 min.	60	30.0	43.0	56.0	
Curve III		30 "	70	60.0	76.0	89.5	
Chart III		45 "	52	66.0	87.0	99.0	
		60 "	28	67.0	88.0	100.5	
		75 "	19	60.0	83.0	93.5	
Miss L. D.	Oct. 16	Fasting	..	4.0	13.0	66.4	10 mg. a day for
See:		10 min.	110	3.8	7.8	21.5	140 days.
Curve IV		20 "	105	8.4	13.4	38.0	
Chart III		30 "	85	22.8	32.4	66.5	
		40 "	65	34.8	43.8	74.5	
		50 min.	52	43.2	52.8	83.0	
		60 "	20	36.4	47.4	92.0	
		70 "	20	19.8	28.4	84.0	
		80 "	14	13.4	22.4	80.0	
		90 "	2	4.4	9.0	67.5	
Miss L. D.	Oct. 18	Fasting	..	12.0	17.0	63.5	Two days later
See:		10 min.	85	0.0	6.5	37.5	therapy un-
Curve V		20 "	65	28.4	35.4	54.0	changed.
Chart III		30 "	63	49.0	60.0	81.5	
		40 "	62	55.6	69.4	93.0	
		50 "	47	63.6	76.6	100.0	
		60 "	37	55.2	69.2	99.0	
		70 min.	19	47.4	58.8	95.0	
		80 "	10	38.4	52.0	92.0	
		90 "	2	33.8	45.6	90.0	

TABLE VII.—PANCREATIC ENZYME ACTIVITY AFTER IRRADIATED ERGOSTEROL THERAPY.

Case III.	Date, 1929.	Pancreatic enzyme.			Irradiated ergosterol dosage.
		Proteolytic.	Lipolytic.	Amylolytic.	
Miss L. D.	Oct. 19	1.72	1.53	2.64	After receiving 10 mg. a day for 140 days.

CASE IV.—Mrs. M. B., aged fifty-four years, a convalescent from osteoporosis, was also studied before and after irradiated ergosterol therapy. She received 5 mg. a day from May 17 to June 11, 1929 (twenty-five days), 8 mg. a day until June 15 (four days), and 20 mg. a day until June 22, 1929 (seven days). During these thirty-six days we noted no untoward symptoms. Here again there is a suggested reduction in the gastric acidity after such vitamin D therapy, but it is not marked enough to call a true effect. No duodenal analyses were performed on this patient.

TABLE VIII.—GASTRIC ANALYSES BEFORE AND AFTER IRRADIATED ERGOSTEROL ADMINISTRATION.

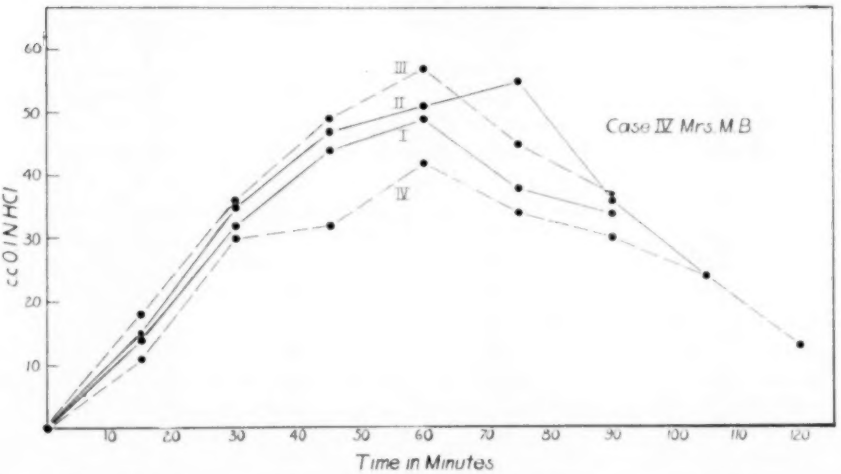
Case IV.	Date.	Time.	Vol., cc.	Free HCl, cc. 0.1 N per 100 cc.	Total acidity, cc. 0.1 N per 100 cc.	Chlorids, cc. 0.1 N per 100 cc.	Remarks.
Mrs. M. B.	May 6	Fasting	73	0	5	47.5	Before therapy.
See:		15 min.	62	14	24	44.0	
Chart IV		30 "	61	32	45	71.5	
Curve I		45 "	41	44	58	87.5	
		60 "	18	49	61	92.5	
		75 "	10	38	53	102.5	
		90 "	2	34	45		
Mrs. M. B.	May 7	Fasting	..	0	5	74.0	Before therapy.
See:		15 min.	80	15	21	41.5	
Chart IV		30 "	75	35	46	67.5	
Curve II		45 "	72	47	62	86.5	
		60 "	55	51	67	94.0	
		75 "	38	55	63	96.5	
		90 "	26	36	55	95.0	
		115 "	12	24	43	92.5	
Mrs. M. B.	June 19	Fasting	10	0	8	51.0	Thirty-two days therapy.
See:		15 min.	74	18	32	71.5	
Chart IV		30 "	86	36	54	72.5	
Curve III		45 "	62	49	67	...	
		60 "	60	57	81	99.0	
		75 "	38	45	66	100.5	
		90 "	2	37	58	97.0	
Mrs. M. B.	June 20	Fasting	25	0	5	64.5	Thirty-three days therapy.
See:		15 min.	104	11	19	35.0	
Chart IV		30 "	88	30	44	59.5	
Curve IV		45 "	72	32	45	68.5	
		60 "	64	42	54	78.5	
		75 "	59	34	49	87.5	
		90 "	19	30	42	91.5	
		105 "	16	24	36		
		120 "	18	13	29	100.5	

TABLE IX.—THE ACID-BASE COMPOSITION OF PANCREATIC JUICE BEFORE AND AFTER IRRADIATED ERGOSTEROL ADMINISTRATION.

Date, 1929.	Pancreatic juice. Cl, cc. 0.1 N.	Pancreatic juice. Calculated HCO_3, cc. 0.1 N.	Pancreatic juice. Determined HCO_3, cc. 0.1 N.	Pancreatic juice. Cl + Calculated HCO_3, cc. 0.1 N.	Pancreatic juice. Cl + Determined HCO_3, cc. 0.1 N.	Pancreatic juice. B., cc. 0.1 N.	Serum. Cl, cc. 0.1 N.	Serum. B., cc. 0.1 N.	Dose per day, mg. irradiated ergosterol.	Weight, kg.	Remarks.
Dog III											
Aug. 8	...	...	...	...	...	...	105.0	160.0	None		
Aug. 10	102.0	44.6	38.4	146.6	140.4	146.6	...	...	None		
Aug. 16	...	...	...	...	...	...	...	...	None	16.5	
Aug. 17	119.0	45.9	45.1	164.9	164.1	164.9	...	...	None		
Aug. 18	117.0	45.6	49.1	162.6	166.1	162.6	...	...	None		
Aug. 19	108.0	44.0	42.4	152.0	150.4	152.0	...	...	None		
Aug. 21	105.0	58.4	54.8	163.4	159.8	163.4	...	...	None		
Aug. 22	...	...	...	...	...	...	99.0	163.0	15	15.4	
Aug. 23	99.0	65.8	60.5	164.8	159.5	164.8	...	...	15		
Aug. 25	94.0	71.4	57.9	165.4	151.9	165.4	...	...	15		
Aug. 27	99.0	66.0	72.6	165.0	171.6	165.0	...	...	15		
Aug. 28	...	...	...	...	...	...	...	159.0	15	14.8	Anorexia.
Aug. 30	110.0	52.8	47.7	162.8	157.7	162.8	...	...	15	...	Vomiting.
Sept. 1	...	...	...	...	...	...	...	...	15	14.0	
Sept. 2	95.0	55.2	59.3	150.2	164.3	150.2	...	...	15	...	Vomiting.
Sept. 3	103.0	47.2	54.4	150.2	157.4	150.2	...	...	15	...	Ergosterol stopped vomiting.
Sept. 4	120.0	42.9	55.4	162.9	175.4	162.9	103.0	162.0	None	...	Vomiting.
Sept. 5	...	...	...	...	...	...	...	...	None	13.2	
Sept. 9	...	...	...	...	...	...	...	...	None	...	Died.
Average values:											
Before therapy	110.0	48.0	46.0	158.0	156.0	158.0	105.0	160.0	...	16.5	
After therapy	100.0	60.0	59.0	160.0	159.0	160.0	103.0	162.0	...	13.2	
Dog V											
Aug. 21	100.0	71.3	70.0	171.3	170.0	171.3	109.0	170.0	None		
Aug. 23	95.0	78.2	42.6	173.0	138.6	173.0	...	...	None		
Aug. 26	85.0	48.3	68.8	153.3	133.8	153.3	...	...	None		
Aug. 28	...	...	...	...	...	...	...	...	15	...	Dog chewed off tip of delivery tube.
Aug. 30	...	...	...	...	...	...	...	...	15	...	Reinserted under ether anesthesia.
Aug. 31	59.0	99.2	96.8	158.2	155.8	158.2	...	...	15	...	
Sept. 3	75.0	76.0	73.4	151.0	148.0	151.0	...	...	15		
Sept. 7	91.0	80.0	74.8	171.0	165.8	171.0	...	...	15	...	Vomiting.
Sept. 9	...	...	...	...	...	...	...	...	None	...	Ergosterol stopped.
Sept. 10	96.0	79.4	73.5	175.4	168.5	175.4	108.0	172.0	None		
Average values:											
Before therapy	93.0	70.0	54.0	163.0	147.0	163.0	109.0	170.0			
After therapy	80.0	84.0	80.0	164.0	160.0	164.0	108.0	172.0			

The Acid-base Composition of Pancreatic Juice Before and After Irradiated Ergosterol Therapy in Dogs. Following the operative procedure described by Elman and McCaughan[11] and used by Gamble and McIver[12] the duct of Santorini was cannulized in each of 5 dogs. Provision was made to collect the pancreatic juice in a sterile balloon outside the abdomen, thus enabling us to make a collection from day to day during the control and irradiated ergosterol administration periods. Only 2 dogs survived the operative and convalescent periods. During the period of study frequent estimations were made of chlorid, carbon dioxid and fixed base content of the pancreatic juice, and occasionally, like determinations were made on the serum. The methods used in making the determinations have been fully described.[9, 13, 14]

CHART IV.—SHOWING THE EFFECT OF IRRADIATED ERGOSTEROL ADMINISTRATION ON THE SECRETION OF FREE HYDROCHLORIC ACID.



Curves I and II represent the values obtained before therapy. Curve III represents values found on the thirty-second day of irradiated ergosterol therapy. Curve IV was obtained on the following day.

RESULTS. The data obtained from the study of Dogs III and V are presented below:

Dog III. The pancreatic duct was cannulized (using ether anesthesia) on August 8, 1929. The postoperative convalescence was uneventful. Control pancreatic juice samples were analyzed from time to time up to August 22, 1929. On this day he began receiving irradiated ergosterol by mouth, 15 mg. a day. On August 22 anorexia was first noted; this was followed in a few days by vomiting and diarrhea. Ergosterol therapy was discontinued on September 4. The animal died five days later. At necropsy an extensive bronchopneumonia was found. The pancreas was small, hard and nodular. The collection tube was still in the duct of Santorini. There was no evidence of peritonitis. In Table IX and Chart V are shown the results of this experiment.

Average values:										
Before therapy	93.0	70.0	54.0	163.0	147.0	163.0	109.0	170.0
After therapy	80.0	84.0	80.0	164.0	160.0	164.0	108.0	172.0

Dog V. The operation was performed under ether anesthesia on August 19, 1929. After a control period of eight days, irradiated ergosterol was given orally, beginning August 28, 1929, in doses of 15 mg. a day. Since the dog began vomiting on September 9, the drug was discontinued on September 10, 1929. In Table IX are tabulated the chemical studies on this dog. (See also Chart V.)

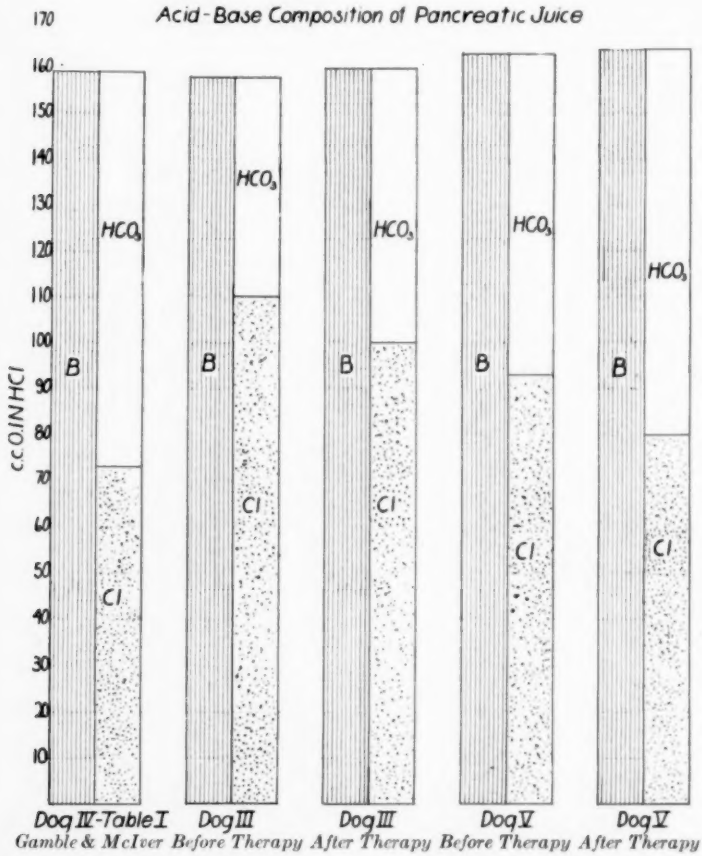


CHART V.—GRAPHIC REPRESENTATION OF THE CHANGES OBSERVED IN PANCREATIC JUICE FOLLOWING THE ADMINISTRATION OF IRRADIATED ERGOSTEROL.

Our normal values (Dog. III and V before therapy) are compared with those of the normal dog (IV, Table I) reported by Gamble and McIver.[12]

From Table IX one notes that the fixed base of the pancreatic juice from each dog was remarkably constant throughout both experiments. The averages for fixed base in the series of samples of pancreatic juice from Dog III and Dog V showed a real difference, being respectively 158 cc. $\frac{N}{10}$ and 165 cc. $\frac{N}{10}$ per 100 cc. (average control period values). There was no change in these values during

the administration of irradiated ergosterol; Dog III showed 160 cc. $\frac{N}{10}$ per 100 cc. and Dog V 164 cc. $\frac{N}{10}$ per 100 cc. The constancy of these values, as well as the differences between the 2 animals, confirms the work of Gamble and McIver.[12]

Gamble and McIver[12] demonstrated that the acid equivalent of the fixed base of pancreatic juice is composed almost entirely of chlorid and carbonate, the phosphate content being so small it is unnecessary to determine it. Therefore, we contented outselves with determining only chlorid and carbonate content in order to determine the acid constituents of the pancreatic juice studied. The samples of pancreatic juice were not collected under oil, and this may account for the wide variations in carbonate content (*"determined"*) seen in Table IX. The sample of juice was shaken in the van Slyke apparatus with alveolar air from the operator and then the carbonate determined. Because of the wide differences in our series of determined carbonate values, we have calculated the expected carbonate value by subtracting chlorid from fixed base. This is spoken of as *"calculated"* HCO_3. In all probability the calculated HCO_3 is much more accurate than the determined HCO_3, because the chlorid method used is a very accurate determination. We feel justified in making such a calculation because the only other acid ion present in pancreatic juice in appreciable amounts is HCO_3.

In Dog III, before irradiated ergosterol therapy, the average value for chlorid was 110 cc. $\frac{N}{10}$ per 100 cc., whereas after such therapy it was 100 cc. $\frac{N}{10}$ per 100 cc. As the chlorid fell, the carbonate rose, the average values being 48 cc. $\frac{N}{10}$ and 58 cc. $\frac{N}{10}$ respectively (calculated HCO_3). Similar results were obtained in Dog V. Here the Cl fell from 93 cc. $\frac{N}{10}$ per 100 cc. to 80 cc. $\frac{N}{10}$ per 100 cc. Coincident with the shift in Cl, the HCO_3 rose from 70 cc. $\frac{N}{10}$ per 100 cc. to 84 cc. $\frac{N}{10}$ per 100 cc. (calculated values). Gamble and McIver[12] stated that the fixed base of pancreatic juice is a much more stationary value than is the chlorid ion and the above results seem to substantiate such a statement.

It will be seen from Table IX that the occasional serum base determinations agree very well with the fixed base values of the pancreatic juice on the same day. This is in agreement with the findings of Gamble.[12] The operative procedure, diet (milk and bread), anorexia, vomiting as well as the irradiated ergosterol therapy, were without effect on either the fixed base or chlorid of the serum. Thus the changes observed in the acid-base composition of pancreatic juice would seem to be a true effect, resulting from irradiated ergosterol administration.

Discussion. In the introduction of this paper we pointed out that certain accumulated evidence suggested that perhaps the *modus operandi* of vitamin D therapy was by way of affecting either the gastric or pancreatic secretions. Other evidence led us

to believe that any changes found would probably be a shift in the reaction of these secretions toward the acid side. These expectations were obviously incorrect, for:

The administration of irradiated ergosterol in man depressed the secretion of free hydrochloric acid. The effect would seem to bear a direct relation to the amount given, because in the case of Mr. R. L. (Case I) a dose of 30 mg. a day resulted in an abnormally low free hydrochloric acid secretion. When he was receiving 5 mg. a day, the reduction in free hydrochloric acid secretion was not so marked, yet definite. This relationship would seem to be borne out in the other individuals studied. We feel justified in concluding that these results are a true effect caused by the administration of irradiated ergosterol, as we were dealing with apparently normal people living under normal conditions, receiving an adequate diet in every respect, and ergamin acid phosphate was given with each test to insure maximal gastric secretion.

Only one case, Mr. D. C. (Case II), showed decreased activity of the pancreatic enzymes as a result of irradiated ergosterol therapy. This depression of pancreatic enzyme activity may have been the cause of the increased number of bowel movements observed in this individual.

The changes in the acid-base composition of the pancreatic juice were definite. Although the fixed base remained stationary, the chlorid content fell and the carbonate value rose with a resulting pancreatic juice which was more alkaline. Because the irradiated ergosterol administration resulted in anorexia, vomiting and loss of weight, one might contend that these results are due to an overdose of the drug. Perhaps they are. Nevertheless, the changes in pancreatic juice are due to its administration.

Depression of free hydrochloric acid secretion and an increase in the alkalinity of the pancreatic juice would result in a decreased acidity of the gastrointestinal tract and thus tend to hinder calcium absorption. Therefore, the *modus operandi* of irradiated ergosterol cannot be due to an increased acidity of the intestinal tract secondary to changes in the composition of gastric or pancreatic juice. The only other ways in which the gastrointestinal acidity could be increased are: (1) The intestines might secrete a more acid succus entericus or, (2) the permeability of the intestinal wall might be altered and thereby allow more complete absorption of calcium and other basic ions. Further study is necessary to prove either of the last 2 mentioned modes of action.

Our results are definite and seem sufficiently important to be recorded. Such studies should be carried out over longer periods of time. Could a complete achlorhydria be produced by irradiated ergosterol? If so, the physiological and clinical significance is evident.

Summary. 1. Irradiated ergosterol administration to 4 individuals produced a reduction in the free hydrochloric acid secretion in 3 cases and a questionable reduction in a fourth.

2. Pancreatic enzyme activity was depressed in 1 individual following irradiated ergosterol administration.

3. Results obtained by Gamble and McIver[12] were confirmed concerning the acid-base composition of the pancreatic juice of dogs.

4. Irradiated ergosterol therapy had no effect on fixed base content of pancreatic juice. It did cause a fall of the chlorid ion and a rise in the carbonate ion and thereby a more alkaline pancreatic juice.

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TREATMENT OF MENINGOCOCCUS MENINGITIS BY CISTERNA PUNCTURE.

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We present herein an analysis of 50 cases in which specific serum was given by the cisterna route, as contrasted with 48 cases treated by the older accepted lumbar-puncture method, the treatment in both series being augmented by the usual intravenous injections of antimeningococcus serum. Every case treated was a proven case of true meningococcus meningitis, the organism being found present as Gram-negative intracellular diplococci in smears of the spinal fluid.

Cisterna puncture has been looked upon as a most unusual and difficult procedure, and its employment in the past was generally limited to cases that were *in extremis*, or in which occurred a high spinal-fluid block, resulting in a dry or gelatinous lumbar tap. Much time was frequently lost before arriving at a decision to puncture the cistern, and then still more in obtaining some one willing to carry out the procedure.

Inasmuch as the portal of entry of the meningococcus into the human body is generally accepted as being through the nose and throat, it would seem logical to suppose, that in the majority of instances, meningitis results by an extension through the numerous orifices for the transmission of the various branches of the olfactory nerve with their attendant vessels, through the cribriform plate. This method undoubtedly occurs in meningitis due to the pyogenic group by extension from the ethmoids and sphenoids in cases of sinusitis without septicemia, and has been observed many times by us. *A priori*, and taking into account the many factors already worked out with reference to meningococcus infection, it seems logical to believe that this is the common method by which the meninges of the brain and cord become involved in meningitis. At any rate, autopsies on cases of the latter type have uniformly shown greatly dilated ventricles containing purulent fluid, with a fibrinopurulent exudate, most marked at the base of the brain, but likewise occurring beneath the pia arachnoid of both cortex and spinal cord.

The cerebrospinal fluid is formed in the choroid plexus of the fourth ventricle of the brain and any loss of this fluid must be

physiologically restored from this source, passing from the ventricle downward into the subarachnoid space of the cord to become the so-called fluid.

Taking into consideration the above circumstances, coupled with the facts that we were having a higher death rate than usual, and were encountering considerable difficulty in many cases with the usual lumbar-puncture treatment, it seemed logical to replace the latter by routine cisterna puncture from the very first treatment. Having a few unrecovered cases in the hospital, lumbar treatment was discontinued and cisternal treatment substituted. Only beneficial results were observed, and since September 1, 1929, lumbar puncture has been entirely replaced by cistern puncture alone. To date over 700 cistern punctures have been done on this service. These include many other cases not reported in this paper, as well as other diseases beside meningococcus meningitis. So far no untoward results have been observed and patients who have had both lumbar and cistern punctures carried out on them, invariably request the latter. Moreover, we find in comparing the two methods, that fluid is much easier and more constantly obtained by the cisternal route. Occasionally the first few drops of fluid obtained are bloody. This is nearly always due to bleeding along the needle from one of the tiny vessels of the muscle, and moving the needle a little to one side or the other nearly always stops it.

Our procedure in doing a cisterna puncture differs in certain respects from other published accounts, and its simplicity we believe warrants a description of these differences. The landmarks are located and the needle introduced as described in all standard accounts. However, the gauge of the needle used is determined entirely by the type of case being treated. If we have reason to believe that the spinal fluid is purulent, we invariably use a large-gauge needle whether the patient be a child or an adult. The use of such a large-gauge needle facilitates drainage and the injection of the serum, a useful procedure in a struggling patient, and nearly always impossible if a small needle be used. We do not measure off a certain distance on the needle's shaft by which to limit its insertion, as we feel that the great amount of individual variation in the thickness of the neck in children, as well as in adults, precludes an arbitrary statement concerning how far it should be inserted. We feel rather that frequent examination by withdrawing the stylet, while gently inserting the spinal needle a short distance at a time, guides us much more accurately in judging the exact location at which the cistern is entered, and is a less dangerous procedure than depending upon a measured distance along the shaft of the needle.

We shall consider first the 48 cases treated by lumbar puncture. These cases were treated immediately preceding the institution of the routine cisternal method, and occurred during the period July 1, 1928 to September 1, 1929. A few of these cases also received one or

Analysis of Data.

Pt. No.	Days ill before entrance	General condition.	Type of puncture.	Spinal fluid cell count.	Result.	No. cc. serum		No. of punctures.	Remarks.
						Thecal.	Vein.		
67-375	4	Fair	Spinal	2,400	Cured	425	90	13	Block, last 2 *via* cistern.
68-553	7	Fair	Spinal	3,700	Cured	225	45	10	Wassermann 4.
79-889	?	Fair	Spinal	3,500	Cured	220	120	15	Age six months.
56-979	5	Fair	Spinal	3,100	Cured	175	65	9	Last 3 punctures *via* cistern with washing.
80-627	12	Poor	Spinal	1,450	Cured	143	100	10	
81-550	3	Fair	Spinal	13,750	Cured	470	220	17	
67-068	3	Poor	Spinal	....	Cured	355	...	18	
83-692	2	Poor	Spinal	4,370	Died	135	105	4	Last puncture *via* cistern.
84-925	4?	Poor	Spinal	243	Died	175	154	14	Last 7 punctures *via* cistern. Age, two months.
67-058	1?	Poor	Spinal	....	Died	625	15?	28	Recurrent type.
67-379	3	Poor	Spinal	6,700	Died	120	90	4	Wassermann 4.
75-720	1?	Poor	Spinal	40,000	Died	45	30	2	In hospital nine hours.
80-788	5	Poor	Spinal	17,000	Died	590	110	27	Last 3 punctures *via* cistern
81-101	1	Poor	Spinal	34,000	Died	385	180	15	Laminectomy for needle. Last 3 punctures *via* cistern.
81-140	4	Poor	Spinal	3,500	Died	350	225	12	Last 3 punctures *via* cistern.
60-933	4	Poor	Spinal	9,000	Died	440	?	22?	Last 3 punctures *via* cistern. Recurrent type.
79-481	3	Poor	Spinal	9,000	Died	45	100	2	Wassermann negative, Kahn 4.
74-625	2	Fair	Spinal	12,200	Died	450	240	18	
74-010	5	Poor	Spinal	24,000	Cured	260	120	11	Eighth nerve left deafness.
73-453	12	Fair	Spinal	240	Died	15	..	1	
73-053	7	Fair	Spinal	1,400	Cured	170	25	9	
71-350	?	Poor	Spinal	360	Died	60	...	1	Patient in hospital fourteen hours.
49-871	?	Poor	Spinal	7,200	Died	55	...	2	
24-107	2	Poor	Spinal	11,200	Died	90	50	1	
261-126	3	Poor	Spinal	1,800	Cured	235	60	14	
26-834	6	Poor	Spinal	4,400	Cured	305	...	?	
28-627	2	Poor	Spinal	....	Died	120	100	5	
32-540	7	Fair	Spinal	5,000	Cured	120	...	7	Wassermann 4.
34-256	12	Fair	Spinal	800	Cured	150	65	8	
35-454	2	Poor	Spinal	200	Died	190	...	8	
36-203	3	Poor	Spinal	60,000	Cured	300	50	12	
39-781	?	Poor	Spinal	17,000	Died	25	15	2	
42-406	3	Fair	Spinal	850	Cured	405	15	11	
41-452	2	Poor	Spinal	20,000	Died	75	115	3	
41-683	4	Fair	Spinal	5,800	Cured	315	85	11	Paralysis of right external rectus muscle.
63-008	?	Fair	Spinal	1,100	Cured	90	4	..	Right simple mastoidectomy.
42-264	2	Poor	Spinal	4,700	Died	30	50	1	Patient in hospital ten hours.
44-205	6	Poor	Spinal	12,000	Died	75	215	5	Patient came in about one month after apparent cure and died of internal hydrocephalus due to meningitis.
44-258	2	Poor	Spinal	....	Died	45	30	2	In hospital two hours.
49-311	14	Fair	Spinal	2,500	Cured	170	50	6	
49-424	2	Poor	Spinal	2,900	Died	30	50	1	In hospital nine hours.
50-450	10	Fair	Spinal	50	Cured	175	...	7	
53-497	3	Poor	Spinal	2,000?	Died	255	150	9	
54-939	3	Poor	Spinal	21,000	Died	60	130	2	Laminectomy to remove broken spinal needle.
58-747	7	Poor	Spinal	9,350	Died	35	55	2	
60-409	2	Poor	Spinal	30,000	Died	170	65	8	
42-688	..	Fair	Spinal	....	Died	165	15	11	Age five months.
43-098	..	Fair	Spinal	1,600	Cured	90	3		
88-813	..	Poor	Cistern	....	Cured	105	85	7	
88-295	3	Poor	Cistern	4,000	Cured	175	180	6	
87-889	6	Poor	Cistern	1,400	Cured	80	45	6	
87-508	3	Poor	Cistern	5,400	Cured	125	157	7	
86-382	5	Fair	Cistern	6,800	Cured	210	305	9	Wassermann 4, "spotted" type. Paralysis right external rectus muscle--eye.

ANALYSIS OF DATA.—(*Continued.*)

Pt. No.	Days ill before entrance	General condition.	Type of puncture.	Spinal fluid cell count.	Result.	No. cc. serum.		No. of punctures.	Remarks.
						Thecal.	Vein.		
86–044	5	Fair	Cistern	4,700	Cured	160	288	11	Wassermann 4.
85–681	3	Fair	Cistern	2,000	Cured	225	90	9	
97–527	7	Poor	Cistern	17,000	Cured	120	230	7	Sent in as psycho case.
85–163	8	Poor	Cistern	....	Died	30	30	1	Patient in hospital one hour and forty minutes.
88–243	3	Poor	Cistern	7,000	Died	75	105	3	
85–811	2	Fair	Cistern	4,000	Died	150	170	5	
88–669	3	Poor	Cistern	11,500	Died	60	70	2	
97–862	3	Fair	Cistern	22,500	Cured	90	170	5	
85–267	7	Fair	Cistern	280	Cured	150	55	7	This patient preferred cistern to spinal.
88–780	3	Fair	Cistern	2,000	Cured	270	90	12	
98–829	2	Poor	Cistern	250	Died	30	...	1	Patient in hospital 6 hours.
90–667	..	Poor	Cistern	43,000	Died	30	30	1	Patient in hospital twelve hours.
89–739	4	Poor	Cistern	....	Died	25	50	1	Patient in hospital sixteen hours.
89–730	..	Poor	Cistern	1,000	Died	40	100	2	
95–853	3	Fair	Cistern	4,000	Cured	120	95	7	
95–832	1	Fair	Cistern	9,600	Cured	187	290	10	
95–671	12	Fair	Cistern	1,200	Cured	105	60	7	
94–882	1	Poor	Cistern	1,700	Cured	165	118	10	
92–979	2	Fair	Cistern	12,000	Cured	145	30	7	
92–402	2	Poor	Cistern	12,000	Cured	115	90	6	
91–984	3	Fair	Cistern	1,200	Cured	178	162	7	
91–769	2	Fair	Cistern	3,500	Cured	115	120	7	
90–389	3	Fair	Cistern	9,500	Cured	235	230	10	Patient had 2 spinal punctures with serum.
90–248	?	Fair	Cistern	800	Cured	75	50	5	
85–678	?	Poor	Cistern	5,000	Cured	275	290	11	Wassermann 4.
103–619	3	Poor	Cistern	16,000	Died	135	165	7	
103–554	3	Poor	Cistern	14,000	Cured	136	85	8	
101–687	5	Poor	Cistern	11,700	Died	40	40	1	In hospital two hours.
101–458	4	Fair	Cistern	3,000	Cured	100	170	6	
101–278	2	Poor	Cistern	16,000	Died	45	100	2	
100–025	5	Fair	Cistern	....	Cured	135	130	8	
99–648	3	Poor	Cistern	15,000	Cured	135	90	5	
99–193	2	Poor	Cistern	75	Died	110	200	6	
99–043	5	Poor	Cistern	8,000	Died	45	80	2	
98–061	5	Poor	Cistern	390	Died	15	35	1	Patient in hospital thirteen hours.
91–240	7	Poor	Cistern	3,900	Died	232	218	16	
89–607	3	Poor	Cistern	2,000	Died	30	45	2	
88–812	..	Poor	Cistern	3,000	Died	340	225	15	Bronchial pneumonia and pleural effusion.
88–542	6	Poor	Cistern	1,000	Cured	145	30	5	Blind before admission. Bilateral meningitis uveitis.
76–977	7	Poor	Cistern	....	Died	330	230	10	Also had 8 spinal. Had lumbar abscess.
103–142	?	Poor	Cistern	6,250	Cured	135	105	8	
7–704	2	Poor	Cistern	6,000	Cured	309	350	10	
95–670	10	Fair	Cistern	1,000	Cured	120	45	8	
105–903	2	Fair	Cistern	6,000	Cured	205	...	8	
69–233	2	Poor	Cistern	10,000	Cured	180	10	7	Nine-months-old baby.

more cistern punctures, when they were *in extremis*, in a desperate effort to save them, and a very few recovered, but inasmuch as the main treatment had been carried out by the lumbar route, for the sake of fairness, we have classed them all as lumbar cases. An analysis of these cases follows:

1. An average of 8.4 punctures was received by each patient for treatment purposes.

2. An average of 200 cc. of antimeningococcus serum was given intrathecally, and 95 cc. was given either intravenously or intraperitoneally, an average total of 295 cc.

3. An average of 25% longer time was spent in the hospital by these cases than those treated by cisterna puncture.

4. Of the 48 cases treated, 28 died, a mortality of 58.3%. Six of these cases were sent to the hospital *in extremis* and died in less than twenty-four hours after admission. If we subtract these cases as having been seen too late to be amenable to treatment, we have remaining 42 cases theoretically curable, and of these 22 died, a mortality of 52.3%. As the 6 cases mentioned were in the hospital an average of only nine hours, their omission seems a fair procedure.

The 50 cases treated by cisterna puncture furnish the following data:

1. An average of 6.4 punctures was received by each patient for treatment purposes, or 2 less than by the lumbar method.

2. An average of 135 cc. of antimeningococcus serum was given into the cistern, and 128 cc. was given either intravenously or intraperitoneally, a total of 263 cc. per case, or 30 cc. less than was used when treating by the lumbar method.

3. Of the 50 cases treated, 18 died, a percentage of 36, which presents a difference in mortality of 22% in favor of the cisternal route. If 7 cases dying in less than twenty-four hours after being hospitalized be subtracted, a still greater percentage exists in favor of the cisternal method. This leaves 11 deaths occurring in 43 cases treated, a mortality rate of 25.5%, or a difference of 27% less than by the lumbar method.

The routine employment of cisterna puncture has removed the former fear of a cord block in the treatment of severe purulent cases. We also use it in the treatment of poliomyelitis, tetanus, and any other condition in which it may seem indicated, frequently employing it by preference for diagnostic purposes. All interns are taught to employ it, at first under close supervision, later by themselves, for any system is of value only when capable of uniform employment. So far no accidents, and only minor difficulties have ever been encountered, and should we be unfortunate enough to occasionally encounter one, we should still feel justified in advocating the method in view of the greater number of lives saved by its use.

Summary. 1. Fifty cases of epidemic meningitis were treated with antimeningococcus serum by lumbar puncture and 48 by cisternal puncture. (2) Analysis of data shows that those treated by the cisternal route have at least a 22% better chance to survive than those treated by the lumbar route, and they require only three-quarters of the time in the hospital; 30 cc. less serum was required; and an average of 2 less punctures is necessary.

REVIEWS.

THE PATHOLOGY OF INTERNAL DISEASES. By WILLIAM BOYD, M.D., M.R.C.P., ED., DIPL. PSYCH., F.R.S.C., Professor of Pathology in the University of Manitoba. Pp. 888; 298 illustrations. Philadelphia: Lea & Febiger, 1931. Price, $10.00.

THE object of this treatise is made clear in the preface: "These pages are devoted to pathologic matters, but *the relation of symptoms to lesions* concludes the discussion of every subject of major importance. In some ways, indeed, it is an illustrated textbook of Internal Medicine, written from the point of view not of diagnosis or of cure, but of the mechanism of disease, its why and its wherefore. . . . In the pursuit of this object the author has not confined himself to the strict limits of morbid anatomy, but has allowed himself to wander rather freely in the realms of pathologic physiology." The Reviewer believes that Professor Boyd has indeed attained his object. The text is clearly written, the numerous illustrations are excellent, and the author has largely limited himself to those diseases which are found in the medical wards of a teaching hospital. An honest attempt has been made to correlate disturbances of structure with disturbances of function. At the end of each chapter there is a good list of references, almost all of them to recent English and American publications. The book is very readable. The author has succeeded in presenting an historical background in a few well chosen lines. For example in his discussion of Bright's disease he says "It is now just one hundred years since there was admitted into Guy's Hospital under the care of Richard Bright an intemperate sailor by the name of John King suffering from edema, scanty urine and albuminuria. The autopsy showed edema of the lungs, pleural effusion, acute pericarditis, an enlarged heart, ascites and small granular kidneys. With the touch of the master, Bright laid his finger upon the kidneys as the seat of the primary disease, and in 1827 published this and many other cases in his celebrated book. . . ." The Reviewer holds that the value of such historical notes cannot be overestimated in giving perspective to the reader, and in making the subject vivid and interesting.

The classification of disease processes, ever a matter of opinion, is in general modern. Probably no two writers would at the present time agree as to the best term for that form of cirrhosis of the liver. variously known as atrophic cirrhosis, hobnailed liver, portal cirrhosis, and so forth. But it is regrettable that Professor Boyd

has chosen the term alcoholic cirrhosis as the most suitable, though he specifically points out that the rôle which alcohol plays in the etiology of this form of cirrhosis is far from clear. While it is most desirable to classify disease on an etiologic basis, it would appear more desirable to retain descriptive names whenever the etiology is unknown. The Reviewer would hasten to emphasize that he has expressed an opinion and not an adverse criticism.

As stated above this book deals particularly with diseases that are met by the student of Internal Medicine. There are included, and rightly so, the diseases of the nervous system. Indeed over 150 pages are devoted to this subject which is only too often treated as the neglected stepchild in books on pathology.

The volume can warmly be recommended to students and practitioners of medicine; to the former as an excellent textbook, to physicians as a reference work of sound value. B. L.

A Text-book of Pathology. Edited by E. T. Bell, M.D. Pp. 627; 316 illustrations. Philadelphia: Lea & Febiger, 1930, Price, $8.00.

This book is the collaborative work of four members of the Department of Pathology and of the Professors of Hematology and of Neuropathology and Neurology in the University of Minnesota. It is edited by the professor of pathology in the same university, who in the preface states that this volume represents an attempt to present the essential facts of pathology to medical students. Because of the confused nomenclature of disease the authors have proposed classifications "which correspond to clinical entities but at the same time are based on etiology and pathology." The present Reviewer would hold such an attempt to reclassify disease praiseworthy but at present wasted effort. Our present day knowledge of etiology and pathogenesis is still in its infancy. The book contains over 300 illustrations, many of them of unusual excellence. The text is clearly and well written, and compares favorably with the several excellent American textbooks of pathology now in current use. The chapter on the diseases of the kidney by Professor Bell, and on diseases of the blood by Professor Downey are particularly attractive since they represent much original work of these two well-known writers. Certain other subjects appear to be but briefly treated. Thus Chapter II on mechanical injuries covers less than three pages; phagocytosis is discussed on one page; pulmonary tuberculosis in four pages. The references given at the end of the various chapters are excellent and direct the reader's attention to a few carefully selected readily accessible papers of lasting value. While this book will probably not supplant any of established

treatises on pathology, it has much merit, and should prove useful not only to the medical student for whom it is primarily written, but to the practitioner of medicine as well. In the opinion of the Reviewer its greatest merit lies in the concise and clear statement of what the several authors consider the *essentials* of pathology.

B. L.

STALKERS OF PESTILENCE. By WADE W. OLIVER, M.D., Introduction by THEOBALD SMITH, M.D., PH.D. Pp. 251; 23 illustrations. New York: Paul B. Hoeber, Inc., 1930. Price, $3.00.

THE author has well accomplished the task that he set himself of tracing "the historical development of man's ideas of the nature of infectious diseases." This in itself prepares one for a broader treatment than the title suggests, so that one should not be surprised at the inclusion of Aristotle, the Methodists, Geber, Roger Bacon, Vesalius and his pupils, Servetus, Harvey, the early microscopists and others who, while undoubtedly contributing magnificently to the fundamentals of medicine, would themselves have been much surprised at being so dramatically dubbed centuries later. Such criticism, which may perhaps be considered as straining at a gnat, is only too frequently justified in days when the desire for "pep" in title and treatment carries even some writers on scientific subjects beyond the facts of the case. Fortunately this latter is not the case of the present booklet and Dr. Oliver has presented in short space a very readable condensation of the high points of medical history with emphasis on infection—the most important of the etiological trinity. The short foreword by Theobald Smith, while fulfilling its object of whetting the appetite for what is to come, leaves one hungering for more *hors d'oeuvres*. E. K.

THE CANDIRU. By EUGENE WILLIS GUDGER, PH.D., with a Foreword by ALFRED SCOTT WARTHIN, PH.D., M.D., LL.D. Pp. 120; 18 illustrations. New York: Paul B. Hoeber, Inc., 1930. Price, $1.50.

AN expansion of an article appearing in the June 1930 number of the *American Journal of Surgery*, this "fish story," told by an ichthyologist, describes a slender South American catfish that enters the urethræ of bathers, especially if they are micturating. Backward pointing spines on the gill covers anchor them so firmly that considerable, even fatal, hemorrhage may result or amputation of the penis be necessitated. Unlikely as the belief appears to be at first sight, the author presents convincing evidence in its favor. The evolutionary aspects of the phenomenon are not discussed.

E. K.

NORMAL FACTS IN DIAGNOSIS. By M. COLEMAN HARRIS, M.D. and BENJAMIN FINESILVER, M.D. Pp. 247, 42 illustrations. Philadelphia: F. A. Davis Company, 1930. Price, $2.50.

IT must be borne in mind that no matter how much we condense them, a given volume of facts remains the same, and that the value of an abridgment depends entirely upon the skill of the abbreviators in selecting and presenting their materials. They should know all of the facts and display good judgment in their arrangement. The material presented in this book represents a very irrelevant and trite collection of details. There is no consistent purpose underlying them, that is, the book is not normal anatomy, physiology or physical examination, but a chaotic and ill assorted mixture of all three. Most of the sentences are as jumbled as the subject matter and the King's English has been so badly treated that even citizens of a republic will not enjoy it. Mistakes are very numerous. A few, such as the incorrect description of Benedict's qualitative test for urinary sugar, must be attributed to careless editing. Other gross faults may be due to excessive abbreviation. However, it is difficult to justify such statements as the following: "The function of the sinuses is said to be that of imparting mass to the face without adding any weight."—"The muscles (of the leg) compose four groups: The extensors, the flexors, the abductors and the calf muscles."—"The male genitalia should be as often inspected and examined as the female genitalia are." It is a pleasure to note in the last sentence quoted a practical application of the much discussed single standard. F. L.

PIONEERS OF PUBLIC HEALTH. By M. E. M. WALKER, with Foreword by SIR HUMPHREY ROLLESTON, BART., G.C.V.O. Pp. 270; illustrated. London and Edinburgh: Oliver and Boyd, 1930. (New York: Macmillan & Co.) Price, 12/6.

ON the facade of the new building of the London School of Hygiene and Tropical Medicine in Gower Street, London—the gift of the Rockefeller Foundation—are the names of the following 21 scientists who have contributed most to the science of public health: Sydenham, Pringle, Lind, Frank, Jenner, Shattuck, Chadwick, Farr, Simon, Pettenkofer, Parkes, Pasteur, Lister, Lewis, Koch, Manson, Laveran, Reed, Gorgas, Biggs and Leishman. It occurred to the mother of a young Cambridge graduate, recently dead in the tropics, that sketches of these benefactors, some unfortunately but little known to posterity, might "interest the passerby in the street." She modestly states that if the reader's interest is stimulated by any of the sketches" sufficiently to send him to the original biographies, their author's object will have been fully attained." She has more

than attained her objective. The simple, readable, yet informative text and the 21 portraits, even without the reference guides to further study at the end of each chapter, are sufficient to stand on their own merits as a permanent contribution to this most creditable and important chapter in the history of human relations.

E. K.

SELECTED READINGS IN THE HISTORY OF PHYSIOLOGY. Edited by JOHN FARQUHAR FULTON, M.D. Pp. 317; 61 illustrations. Springfield, Ill.: Charles C. Thomas, 1930. Price, $5.00.

STIMULATED by Long's similar and equally entertaining "Readings in Pathology" (For review see AM. J. MED. SCI., 1930, **179**, 420), the author has prepared transcripts of a series of original documents that are both fascinating reading in themselves and also most useful as convenient references and as ready aids in stimulating students to familiarize themselves with the great original sources. The Reviewer, well remembering the influence that Camac's "Epoch-making Contributions" had on his early medical days, has little fear of contradiction in asserting that, if the habit of turning to the first writings on given topics was important in those days, it is still more so in this hectic period of unassimilated scientific facts.

The Editor, as he modestly terms himself, has accomplished his task beautifully. Not only is the selection excellent, but his own paragraphs introductory to each section add greatly to the charm of the presentation, while disclosing his masterful grasp with the general field. This familiarity also is evidenced by the boldness of his selections—not hesitating to include the work of living authors, he is thus able to approach a true perspective of the jerky steps by which Physiology has advanced through the centuries and of the importance of the contributions of this generation. Thus in the chapter on Muscle and Peripheral Nerve, there are 8 selections from the present century by authors still living, as compared to 8 for all preceding time. This ratio of course does not hold throughout—analysis of the material shows 3 selections from the ancients; 1 (Servetus) from the sixteenth century; 18 from the seventeenth, 15 from the eighteenth, 25 from the nineteenth (10 of these are in the field of the Central Nervous System), and 26 from the twentieth century. While the editor-author has resisted the temptation of including from adjacent biologic fields representatives who have indirectly contributed to physiology; such as Vesalius in Anatomy, Virchow and Cohnheim in Pathology, Pasteur in Bacteriology and so on, on the side of physics he has been more indulgent. Thus the first 2 selections are Jean Rey's "on the reason why tin and lead increase in weight on calcination" and Robert Boyle's "Defence of the Doctrine Touching the Air." both presumably included on account of their author's important relation to Physical Chemistry

and Chemistry respectively. The list of masterpieces is too long to touch upon in any detail. Suffice it here to say that in the various chapters (1, General Principles; 2, The Circulation; 3, The Capillaries; 4, Respirations; 5, Digestion; 6, Muscle and Peripheral Nerves; 7, The Central Nervous System; 8, Miscellaneous), the whole subject of physiology is adequately covered, though obviously no one selector can completely satisfy all tastes.

The book is prepared in the attractive way to which we are quickly becoming accustomed in the output of this new and energetic publishing house. The 60 illustrations demand a special word of praise: obviously selected with discernment by one who has a fine historical library of his own, they adequately cover the well-known subjects and yet almost without exception with fresh unhackneyed material that would be found with difficulty elsewhere. With the impetus afforded by the success that the two pioneer books merit, we should soon see similar selections from Anatomy, Medicine, Surgery and even from some of the more specialized subjects—the whole constituting another American contribution to medical history of first class importance. E. K.

MONOGRAPHS ON BIOCHEMISTRY. Edited by R. H. A. PLIMMER, D.Sc., and SIR F. G. HOPKINS, M.A., M.B., D.Sc., F.C.S., and Bacterial Metabolism by MARJORY STEPHENSON, M.A., Associate of Newnham College, Cambridge. Pp. 247; 42 illustrations. London: Longmans, Green & Co. Price, 18s., net.

THIS latest addition to the biochemistry monograph series will be welcomed by both bacteriologists and biochemists. It is important to remember that the early studies of Pasteur in bacteriology were made primarily from the biochemical point of view, after Pasteur himself a pure chemist, had studied fermentation and putrefaction, which he proved to be due to the action of living bacteria. Unfortunately following Pasteur came a period in which, on the one hand, the products of bacteria were studied as separate entities apart from the cell of whose metabolism they represented only a fraction, while on the other hand the chemical activities of microorganisms were studied only as they served to differentiate one organism from another. Within the past few years, however, there has been a return to the biochemical attitude toward bacteria and so large a literature has accumulated that bacterial metabolism has become a special field of biochemistry.

Like its predecessors in the series this monograph contains a very complete, readable and scholarly review of the present knowledge in the subject. It deals very fully with such phases of bacterial metabolism as energy relations, respiration, growth and nutrition, carbohydrate and protein metabolism. There is a particularly

interesting chapter on those remarkable and useful organisms the autotrophic bacteria, and another upon the fixation of nitrogen.

In the appendix will be found an excellent drawing and description of the Barcroft differential monometer with full directions for the calibration of this apparatus. Here also are useful formulæ for synthetic culture media, suitable both for general use and for the cultivation of special organisms.

A very complete bibliography is given. E. W.

DISEASES OF THE SKIN. By GEORGE CLINTON ANDREWS, A.B., M.D. Pp. 1091; 988 illustrations. Philadelphia: W. B. Saunders Company, 1930. Price, $12.00.

THIS, the most recent addition to the flock of American dermatological texts, is interesting from a number of points of view. It raises the question, first of all, as to whether there is any justification for a new American textbook of diseases of the skin for practitioners and students. In the opinion of the Reviewer, American dermatological literature needs authoritative monographs on special subjects, a condensed statement, covering the common dermatoses only, of the elementary principles of diagnosis and treatment for practitioners and students; one or more volumes on the medical aspects of dermatology; a volume on investigative principles and methods as applied to dermatology, and a really massive English or American system comparable to the magnificent Jadassohn Handbuch. It seems to the Reviewer that there is already available a sufficient number of textbooks for ordinary instructional purposes.

The author of this text, however, puts a slightly different light on the matter by saying that his intent in writing this text was to bring the subject up to date for himself. Andrews has in large measure achieved his purpose, particularly with reference to the roentgenologic and actinotherapeutic fields. The up-to-dateness of the book in these particulars is refreshing and this fact alone makes it a valuable addition to the medical library. It must be said, however, with equal frankness that the tone of the book as a whole, the material included and the manner of its presentation make it, in the Reviewer's opinion a work primarily for specialists, and near-specialists rather than for practitioners and students. It is a matter for serious question whether either the practitioner or the medical student should be encouraged to believe, from a presentation of this sort, that he is fitted to undertake the more highly developed aspects of dermatologic therapeutics, particularly as they involve Roentgen ray and radium.

The make-up of the book from the standpoint of classification

and description is a welcome relief from the absolutely conventional. There is a good deal of unevenness of presentation and topics which have an important medical background receive a treatment more in accord with the old-line Hebra dermatology than one could wish in view of the more recent advances in knowledge. For example, the consideration of eczema is largely skin-deep and the enormous emphasis placed on contact factors and allergy, while quite in keeping with the trend of the literature of the past decade, leaves, to the Reviewer's mind, still much to be desired, particularly in the presentation of the subject to medical students. Four or five pages of almost impossible exclusion diets could hardly take the place of a penetrating analysis of the etiologic background of eczema. Dermatologists who, after all, must be the judges of a question of therapy, may differ sharply with the author on such points as the Roentgen ray treatment of psoriasis, which to the Reviewer, for example, has always seemed because of its risks, among the weakest and least justified of the uncertain props upon which the treatment of this disease rests at the present day. Here, as in a number of other aspects of the work, the undoubted virtues of Roentgen ray, much more appreciated in this country than abroad, occasionally lead to overenthusiasm. The discussion of the grenz or Bucky rays appropriate to a special monograph on actinotherapy for the specialist has very little place in a work of this sort, intended for practitioners and students.

Having enumerated in this fashion the adverse criticisms, one turns with pleasure to the undoubted merits of this work. The sections of the book which express the personal experience of the authors are full of stimulating and interesting suggestions. Much excellent material has been collected from the literature. Attention to the technical detail, as for example in the treatment of hypertrichosis, is unusual on the part of a dermatologic author and the descriptions here given are often excellent. The treatment of syphilis, however, is described in greater detail than seems appropriate to a dermatologic text, for it is hardly believable that syphilologists, who alone, together, perhaps, with neurologists, should undertake the intraspinal therapy of neurosyphilis, will proceed to inform themselves on the technique from a textbook of dermatology. None the less there is a laudable attention to many technical points which every practitioner and student needs to know in the management of this disease.

The balance between photographs and text has been well maintained and the photographs are excellent. In fact, there are to the specialist a number of figures that have the worth of atlas presentations. The collection of photographs of the various types of poison oak and ivy and the primrose would make useful material for the information of patients in the consulting room. Valuable items of the author's own experience are given, for example, in the cita-

tion of a case of severe prostration with coma as an apparent anaphylactic reaction to a minute dose of rhus tincture by mouth. The format of the work is excellent and the details of proofreading, quality of paper, and binding follow the very high standard characteristic of the publishers. The index is also unusually full.

There can be no mistaking the fact that this book is a good piece of work. J. S.

OUTLINE IN OBSTETRICS FOR NURSES. By F. W. RICE, M.D. Pp. 228; 56 illustrations. St. Louis: The C. V. Mosby Company, 1930. Price, $2.00.

THIS is based on lectures on obstetrics given by the author to nurses over a period of eleven years. This method of presenting to the beginning student the essential facts in a logical arrangement should assist them considerably in retaining practical elements.

The illustrations including photographs, diagrams and sketches are excellent and important as an aid in teaching.

A few blank pages at the end of each chapter for additional notes, give the book a personal value as intimate as a diary.

An introductory chapter on ethics is not inappropriate and a final chapter of fifty review questions cover all important practical knowledge a nurse should have in this subject. M. S.

BOOKS RECEIVED.

NEW BOOKS.

Physics of Radiology. By J. L. WEATHERWAX, M.A., Physicist, Philadelphia General Hospital. With a Foreword by HENRY K. PANCOAST, M.D., Professor of Roentgenology, University of Pennsylvania. Pp. 240; 136 illustrations. New York: Paul B. Hoeber, Inc., 1931. Price, $5.00.

The Factor of Infection in the Rheumatic State. By ALVIN F. COBURN, Resident Physician, Presbyterian Hospital, New York City Pp. 288; 48 illustrations. Baltimore: The Williams & Wilkins Company, 1931. Price, $6.00.

Capital Investment in Hospitals. Publication Number 7. By C. RUFUS ROREM, PH.D., C.P.A. Pp. 43. Washington, D. C., The Committee on the Costs of Medical Care.

Miscellaneous Contributions on the Costs of Medical Care. Number 7, Medical Care in Middletown. By ROBERT S. LYND and HELEN MERRELL LYND. Pp. 11. *Number 8. The Need of Hospitals for Competent Directors.* By MICHAEL M. DAVIS. Pp. 8. Washington, D. C. The Committee on the Costs of Medical Care.

Transactions of the Japanese Pathological Society, Vol. XX, 1930. Pp. 801; illustrated. Tokyo, Japan: The Japanese Pathological Society.

Guy's Hospital Reports, Vol. 80, No. 4, October, 1930. Edited by ARTHUR F. HURST, M.D. Pp. 121; illustrated. London: The Lancet, Ltd., 1930. Price, 12/6, net.

The historical note on Thomas Guy and Hurst's 3 papers on Addison's Anemia are unusually interesting.

The African Republic of Liberia and the Belgian Congo, Vols. I and II. Edited by RICHARD P. STRONG, Department of Tropical Medicine, Harvard University Medical School. Pp. 1064; 468 illustrations and 28 text figures. Cambridge, Mass.: Harvard University Press, 1930.

The Guidance of Mental Growth in Infant and Child. By ARNOLD GESELL, PH.D., M.D., SC.D. Professor of Child Hygiene, Yale University. Pp. 322; illustrated. New York: The Macmillan Company, 1930. Price, $2.25.

A System of Bacteriology in Relation to Medicine, Vol. I, History, Morphology, Physiology. By various authors. Pp. 374; illustrated. London: Medical Research Council, 1930. Price: £1.1.9 for this volume; for the set £8.14.9. Obtainable in the United States at British Library of Information, 5 E. 45th Street, New York.

A System of Bacteriology in Relation to Medicine, Vol. II, Cocci, Hemophilic Bacteria. By various authors. Pp. 420. London: Medical Research Council, 1929. Price: £1.1.9 for this volume; for the set £8.14.9. Obtainable in the United States at British Library of Information, 5 E. 45th Street, New York.

A System of Bacteriology in Relation to Medicine, Vol. V, Glanders, Diphtheria, Tuberculosis, Leprosy, Brucella, Anthrax. By various authors. Pp. 505. London: Medical Research Council, 1930. Price: £1.1.9 for this volume; for the set £8.14.9. Obtainable in the United States at British Library of Information, 5 E. 45th Street, New York.

A System of Bacteriology in Relation to Medicine, Vol. VII. Virus Diseases, Bacteriophage. By various authors. Pp. 509; illustrated. London: Medical Research Council, 1930. Price: £1.1.9 for this volume; for the set £8.14.9. Obtainable in the United States at British Library of Information, 5 E. 45th Street, New York.

The Pathology of Internal Diseases. By WILLIAM BOYD, M.D., M.R.C.P., ED., DIPL., PSYCH., F.R.S.C., Professor of Pathology in the University of Manitoba. Pp. 888; 298 illustrations. Philadelphia: Lea & Febiger, 1931. Price, $10.00.

Traumatotherapy. The Treatment of the Injured. By JOHN J. MOORHEAD, Professor of Surgery and Director, Department Traumatic Surgery, New York Post-graduate Medical School and Hospital. Pp. 574; 625 illustrations. Philadelphia: W. B. Saunders Company, 1931. Price, $7.00.

Abdomino-pelvic Diagnosis in Women. By ARTHUR JOHN WALSCHEID, M.D., Director of Obstetrical and Gynecological Department of Broad Street Hospital. Pp. 1000; 398 illustrations. St. Louis: The C. V. Mosby Company, 1931. Price, $12.50.

A Manual of the Common Contagious Diseases. By PHILIP MOEN STIMSON, A.B., M.D., Associate in Pediatrics, Cornell University Medical College. Pp. 351; 40 illustrations and 2 plates. Philadelphia: Lea & Febiger, 1931. Price, $3.75.

How It Happened. By ADALBERT G. BETTMAN, M.D., F.A.C.S. Pp. 110. Philadelphia: F. A. Davis Company, 1931. Price, $1.00.

Practical Radiation Therapy. By IRA I. KAPLAN, B.S., M.D., Director, Division of Cancer, Department of Hospitals, New York City. With a Special Chapter on Applied *X*-ray Physics, by CARL B. BRAESTRUP, B.Sc., P.E., Radiation Physicist, Division of Cancer, Department of Hospitals, New York City. Pp. 354; 225 illustrations. Philadelphia: W. B. Saunders Company, 1931. Price, $6.00.

Early Theories of Sexual Generation. By F. J. COLE, D.Sc., OXON., F.R.S., Professor of Zoölogy, University of Reading. Pp. 230; 21 illustrations. New York: Oxford University Press, 1930. Price, $6.00.

Through the Alimentary Canal with Gun and Camera. Personally conducted by GEORGE S. CHAPPELL. With an Introduction by ROBERT BENCHLEY. Pp. 231; 18 illustrations. New York: Frederick A. Stokes, 1930. Price, $2.00.

Thomas Say, Early American Naturalist. By HARRY B. WEISS, and GRACE M. ZIEGLER. A Foreword by L. O. HOWARD. Pp. 260; illustrated. Springfield, Ill.: Charles C. Thomas, 1931. Price, $5.00.

The Metabolism of Tumors. Edited by OTTO WARBURG, Kaiser Wilhelm Institute for Biology, Berlin-Dahlem. Translated from the German edition, with accounts of additional recent researches by FRANK DICKENS, M.A., PH.D., Whole-time worker for the Medical Research Council at the Courtauld Institute of Biochemistry, Middlesex Hospital, London. Pp. 327; illustrated. New York: Richard R. Smith, Inc., 1931. Price, $12.00.

NEW EDITIONS.

Modern Surgery. By JOHN CHALMERS DA COSTA, M.D., LL.D., F.A.C.S., Samuel D. Gross Professor of Surgery, Jefferson Medical College, Philadelphia. Pp. 1404; 1050 illustrations. Tenth Edition, revised and reset. Philadelphia: W. B. Saunders Company, 1931. Price, $10.00.

Operative Gynecology. By HARRY STURGEON CROSSEN, M.D., F.A.C.S., Professor of Clinical Gynecology, Washington University School of Medicine, and ROBERT JAMES CROSSEN, M.D., Instructor in Clinical Gynecology and Obstetrics, Washington University School of Medicine. Pp. 1078; 1246 illustrations and 2 color plates. Fourth Edition. St. Louis: The C. V. Mosby Company, 1930. Price, $15.00.

With each edition this book grows in size and excellence. Not only are the various operations described but the preference indicated for the given case. The need for operation, and pre- and postoperative treatment receive careful handling. In this most extensively revised edition 4 new chapters and over 400 illustrations have been added.

A Manual of Normal Physical Signs. By WYNDHAM B. BLANTON, B.A., M.A., M.D., Assistant Professor in Medicine, Medical College of Virginia. Pp. 246; 48 illustrations. Second Edition. St. Louis: The C. V. Mosby Company, 1930. Price, $3.00.

No abnormal signs considered. Use of the modern tabloid style permits a profusion of easily found facts. Better for reference than connected reading or study.

Nosography. The Evolution of Clinical Medicine in Modern Times. By KNUD FABER, M.D., LL.D., Professor of Internal Medicine, University of Copenhagen. With an Introductory Note by RUFUS COLE, M.D., Director of Hospital, Rockefeller Institute. Pp. 222; 22 portraits. Second edition, revised. New York: Paul B. Hoeber, Inc., 1930. Price, $3.75.

The reappearance of this charming book after seven years and in amplified form is most welcome. Not only has much water passed under the mill but the need for emphasis of the importance of nosography still remains great.

Medical Jurisprudence. By ELMER D. BROTHERS, B.S., LL.B., Member of the Chicago Bar. Pp. 309. Third Edition. St. Louis: The C. V. Mosby Company, 1930. Price, $3.50.

This statement from the legal point of view is practically unique in English medical literature and correspondingly valuable.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

JOHN H. MUSSER, M.D.,

PROFESSOR OF MEDICINE, TULANE UNIVERSITY OF LOUISIANA, NEW ORLEANS.

The Number of Formed Elements in the Urinary Sediment of Patients Suffering from Heart Disease, With Particular Reference to the State of Heart Failure.—Several years ago Addis recommended a technical procedure which so concentrates urine that the formed elements are not destroyed. He found that the number of casts for an actual twelve-hour period varied in normal individuals between 0 and 4270, the average being 1040; the number of red blood cells between 0 and 425,000, the average being 65,700; the number of white blood and epithelial cells between 32,400 and 1,835,000, the average being 322,500. The casts were hyalin; granular casts were not observed. STEWART and MOORE (*J. Clin. Invest.*, 1930, **9**, 409) undertook to make a similar study in patients who had heart disease and chiefly in those who had heart disease of the congenital type. The number of casts found in such individuals seemed to bear a distinct relationship to the severity of the heart failure, the greatest number being passed during the acute failure with a reduction of the number after recovery and fewer still in those who had never suffered from this illness. In the 18 patients who were studied, 12 of them exhibited figures higher than the highest known value observed by Addis. The number of red cells in those who never had heart failure was twice as high as that in the normal individual and from 10 to 15 times as great as in normal individuals when these people with heart disease were suffering from heart failure. The number of red blood cells was not above normal in the urine of those who did not have heart faiiure, but the average number was approximately twice that of the normal person and the average was considerably higher in those who had cardiac failure at the time the count was made.

Nucleotide Therapy in Agranulocytosis.—Agranulocytic angina is a disease which is considered by some to be a definite clinical entity; by others merely a depression of the production of granulocytes or of their

delivery into the circulation because of failure of the bone marrow in the course of a toxemia. On this latter basis REZNIKOFF (*J. Clin. Invest.*, 1930, **9**, 381) considered that treatment of the disease might rationally be carried out by the employment of methods for the stimulation of the polymorphonuclear elements. This reaction occurs when certain nucleotides are employed, such as adenin sulphate and guanin hydrochlorid, with both of which when given intravenously there was a marked increase in the granulocytic count of the experimental animal. Three cases of agranulocytosis are reported, together with a full, complete account of the details of the administration of the drugs. In the first patient recovery was prompt following the administration of 0.5 gm. of adenin sulphate in 25 cc. of saline solution every day. In the second case the patient got along very well indeed under similar therapy, but she developed a recurrence of her agranulocytic state and died. Nucleotide was not used in this last attack. The third patient had three or four bouts of oral cavity infection, in each of which she had a rather remarkable blood picture. On June 6 she developed an acute sore throat, during the course of which the polymorphonuclears were 0 per cent and a total count in several instances of under 2000. Adenin sulphate was started and the total count proceeded to rise and the polymorphonuclears to go up to 31 per cent, when suddenly she developed an infection of the left arm with fever for four days, during which the total count rose to 18,000. Fever subsided in a few days and there was no return of the agranulocytic condition. As a result of the recovery of these 3 patients, Reznikoff believes that nucleotide therapy in agranulocytic angina is the rational procedure.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

PHILADELPHIA, PA.

Intracranal Calcification.—COURVILLE and ADELSTEIN (*Arch. Surg.*, 1930, **21**, 801) state that a short general review of the occurrence of intracranial calcification is given with the pathologic possibilities. Calcareous deposit may be found in practically every type of primary intracranial newgrowth, although with the exception of the craniopharyngeal pouch cysts it is probably most common in the gliomas. Hyalin degeneration or other marked regressive changes are not essential to the deposit of calcium in gliomas. It is essentially a chemical rather than a histologic process. The calcareous material is found characteristically in the media and the adventitia of the bloodvessels, occurring to a much less extent in the cells of the tumor and very rarely in the stroma. The association of calcification in small bloodvessels with liquefaction cysts at the margin of the glioma is noted. The presence of calcification is of value in the diagnosis and localization of gliomas and further emphasizes the importance of securing satisfactory roentgenograms

of the skull in every case of suspected intracranial tumor. The distribution of the calcareous material is usually evenly spread throughout the tumor tissue and gives some conception as to its size and relationships. The duration of the symptoms will often suggest the type of glioma that can be suspected. These with a history of from six to twelve months will likely be neurogliablastomas, while those of longer duration will more likely be astrocytes. Because of the small size of the individual masses calcareous material may be present in a glioma and yet fail to appear in the roentgenogram. Roentgen examination usually reveals an associated thinning of the skull over the tumor, indicating a local rather than a general increase in pressure. Calcification in a glioma is an indication of its relative rather than its absolute benignity. A large proportion of the cases showed the variety of glioma considered malignant. The process may apparently occur in any type of the group.

Clinical Evidence on the Question of Movable Kidney.—LEWIS and CARROLL (*J. Urol.*, 1930, **24**, 479) claim that movable kidney is a reality both clinically and pathologically and demands prompt recognition and appropriate surgical relief. Such recognition is to be based on the modern methods of examination described. Diagnosis requires proof on two points in particular: (*a*) As to the presence of unduly movable or displaced kidney, and (*b*) as to whether the symptoms complained of are coming from this displacement or mobility. Methods of relief, are both palliative and surgical; abdominal binders and nephropexy, the latter affording permanent results when properly carried out. Binders are effective only as long as they are worn, no cure or permanent relief being afforded by them. The "fattening" methods of treatment offer no probability of success and are pure waste of time.

Surgical Therapy for Gastric and Duodenal Ulcers.—ST. JOHN (*Ann. Surg.*, 1930, **92**, 597) says that the high mortality in gastroenterostomy in this series is largely due to pulmonary complications. General anesthesia has been used as a rule. Undoubtedly local or spinal anesthesia would have lowered the incidence of pneumonia. The high mortality in partial gastrectomy is probably due primarily to the fact that it has not been performed in simple duodenal or pyloric ulcer, but rather in the advanced penetrating lesions of the pylorus and lesser curvature. Medical treatment by the surgeon has been of educational value. A follow up study in continuity presents illuminating facts, the most important of which is the evidence of fluctuation of result due to intangible factors. These require further investigation. Observations of the result of treatment should not be discontinued at any definite period following operation. It must be borne in mind in comparing surgical and medical results that surgery in most clinics today in simple ulcer is only instituted at the point where medicine has failed.

The Larynx as Related to Surgery of the Thyroid Based on an Anatomic Study.—NORLAND (*Surg., Gynec. and Obst.*, 1930, **51**, 449) state that since Kocker called attention to the possibility of injury to

the superior laryngeal nerve in thyroid surgery and since other observers' findings point to the fact that the interarytenoid muscle is supplied by the internal branch of the superior laryngeal nerve and since the author's dissections indicate that it is easy to injure the superior laryngeal nerve in the ligature of the superior thyroid artery, it is reasonable to conclude that postoperative disturbance to the voice may occur from injury to this nerve in thyroid surgery. Further because the recurrent laryngeal nerves occur anterior to the inferior thyroid arteries, just as frequently on both sides and because they penetrate the thyroid space a little farther from the tracheoesophageal groove than is usually described, therefore, to avoid injury to these nerves, extrafascial ligation of the inferior thyroid artery according to De Quervain, is more reasonable when ligation of this artery is contemplated.

Excision of Duodenal Ulcer.—Judd and Hazeltine (*Ann. Surg.*, 1930, **92**, 563) say that this paper consists of a report of the local operations which have been performed in the Mayo Clinic for duodenal ulcer. Gastroenterostomy will probably remain the popular operation for duodenal ulcer. It is satisfactory in all cases except in those in which secondary ulcers develop and in those in which hemorrhage occurs and in which bleeding may continue. The operation of excision was developed to be used in these cases in which it was possible to carry it out safely with the idea of avoiding jejunal ulcer and possibly reducing the number of cases in which bleeding occurs, after gastroenterostomy for hemorrhagic ulcer. For many years the local operation consisted in excision of the ulcer or destruction of the ulcer by cautery with simple closure of the area in the duodenum. Of late it has been felt that removal of the anterior part of the pyloric sphincter, in addition to excision of the ulcer produced more complete relief from symptoms. With this removal of muscle everything is accomplished that gastroenterostomy can accomplish and in addition, the ulcer is removed. In cases in which multiple ulcers are encountered and in which it is not possible to remove all of them it is probably best to remove the anterior ulcer, close the duodenum and then to complete the operation with gastroenterostomy. The local operation is limited to those cases in which the duodenum is fairly mobile. As one's experience increases with these cases, however, one realizes that it is not difficult to mobilize a duodenum that is fairly well fixed and this should be done in cases in which excision of the ulcer is definitely indicated. Gastroenterostomy is fairly satisfactory for older patients, especially if obstructive symptoms have developed. Gastroenterostomy is less satisfactory in young patients. A study of the immediate results from local operations show that it can be done with very little risk. This report covers 1363 cases with a mortality of 0.44 per cent. The ultimate results in this group of cases are practically the same as the ultimate results obtained by gastroenterostomy; the patients in 90 per cent of the group in which the authors have detailed reports have obtained satisfactory results. The local operation can be performed in about 50 per cent of the cases of duodenal ulcer.

THERAPEUTICS

UNDER THE CHARGE OF

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The Therapeutic Influence of Disturbed Water Metabolism Following the Withdrawal of Morphin.—According to the observations of ADLER (*Klin. Wchnschr.*, 1930, **9**, 2011), considerable water retention may occur during and following the withdrawal of morphin. This retention is associated with decreased urinary output and dilution of the blood. It is suggestive that with the development of morphin addiction the water metabolism is altered; so that when the body fails to receive morphin, disturbance of this morphin regulated water metabolism becomes manifest. In order to correct this condition, the author used euphyllin, a combination of theophyllin and æthylendiamin. This drug was selected because it has both central and peripheral action. In 12 patients euphyllin was administered after the sudden withdrawal of morphin; in 2 additional patients the euphyllin was used while the morphin was gradually withdrawn. Two patients were treated with novasurol after morphin withdrawal, for comparison. The patients received no other medication. The author claims that in the patients treated with euphyllin there were no severe manifestations of morphin withdrawal. Cardiac symptoms were entirely absent. The appetite was good; nausea or vomiting developed only occasionally. The patients got out of bed as early as the second day of treatment and gained weight steadily. The 2 patients who received novasurol developed nausea, vomiting and diarrhea; and the morphin abstinence caused a more severe reaction than that experienced by patients treated with euphyllin. The clinical improvement of the patient did not always run parallel to the reëstablishment of a normal water balance. The duration of the euphyllin treatment varied from two to seven days. Daily amounts of 0.48 gm. intramuscularly, or 0.12 or 0.24 gm. intravenously were administered. Slow intravenous administration of euphyllin is preferable, as the intramuscular injection is painful.

The Treatment of Paralytic Ileus With Vasopressin.—ELMER, PTASZEK and SCHEPS (*Klin. Wchnschr.*, 1930, **9**, 1765) have observed that while the subcutaneous injection of vasopressin markedly increases intestinal peristalsis in experimental animals, oxytocin has but little effect. Comparative observations on isolated loops of intestine show that vasopression increases the peristalsis more than pituitrin. Oxytocin has no effect on the motility of intestinal loops. The effect of

vasopressin is more pronounced on the colon than on the small intestines. When vasopressin and oxytocin are administered simultaneously, the latter exerts an antagonistic effect on the intestinal action of vasopressin. These experimental observations suggest a useful clinical application of vasopressin in paralytic ileus. The authors claim that subcutaneous administration of 10 units of vasopressin increases peristalsis and relieves the abdominal distention of this condition provided there is no obstruction. If this dose is without effect within an hour, a dose of 20 units can be administered. In obstinate cases, if subcutaneous administration fails, 20 units may be given intramuscularly or slowly intravenously. Occasionally untoward side effects, which may manifest themselves as headache, abdominal pains, nausea, pallor and micturition, are observed. The authors claim that the use of vasopressin in paralytic ileus decreases its mortality rate.

The Prevention of Rickets by the Administration of Irradiated Milk to Nursing Mothers.—It is established that the antirachitic principle is transmissible through mothers' milk. SCHEER and SANDELS (*München. Med. Wchnschr.*, September 5, 1930, p. 1543) have performed experiments on rats, and observations on children with rickets which indicate that the mothers' milk increases in antirachitic potency after the consumption of irradiated milk by the mothers. The mothers' milk, after the daily consumption of 500 cc. of irradiated milk, rapidly cures the manifestations of rickets in babies.

A Quantitative Biologic Standardization of Anterior Pituitary Lobe Preparations.—No preparation of a potent and stable extract of anterior pituitary lobe suitable to general practice is available at present, partly because no test of the potency of the positive principle of the pituitary body has been found. A biologic test of the various extracts is made by studying the effect of the extracts: (1) on the growths of animals; (2) on the thyroid and adrenal glands; (3) on the metabolism; (4) on the sexual organs. These biologic tests are mainly qualitative in nature. the quantitative evaluation of the potency of a preparation is difficult to determine, first because of the lack of a potent and stable preparation and second because of a marked variation in the susceptibility of animals. JANSSEN (*Klin. Wchnschr.*, 1930, **9**, 1853) has prepared this needed potent and stable preparation by dehydrating the fresh chopped anterior lobe in water-free acetone. After the removal of the acetone in vacuum, the powdered gland is kept over phosphopentoxid. The potency of the gland is thus preserved qualitatively as well as quantitatively. The powder of 50 glands serves as a standard preparation. The effect of this preparation on the sex glands of female rats was studied, and the ratio between positive and negative responses graphically charted. The author claims that this is a suitable quantitative test of the anterior lobe preparations. He found the standard preparation inactive when administered orally. All commercial preparations tested with the method described proved to be practically ineffective when administered in total doses up to 6 cc.

PEDIATRICS

UNDER THE CHARGE OF

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A Statistical Comparison of Breast-fed and Bottle-fed Babies During the First Year.—FABER and SUTTON (*Am. J. Dis. Child.*, 1930, **40**, 1163) emphasize the limitations which they feel should be placed on the conclusions drawn from their study. They feel that the differences between breast feeding and artificial feeding are representative under the conditions of the survey but not in the absence of them. These conditions favorable to artificial feeding were: an equable climate, conducive to the keeping of milk unspoiled even without ice or mechanical refrigeration, and without the depressing physical effects of extremes of heat and cold; reliable, pure milk; frequent medical supervision of feeding and care, and routine administration at the proper ages of necessary dietary accessories, such as cod-liver oil, orange juice and green vegetables. In addition there were always demanded fresh air and sun baths, and a large proportion of the babies had these in abundance. Most of these can be duplicated in most American communities, but in respect to the usually dependable low mean temperature which delays the bacterial spoilage of milk without special refrigeration, there was present a condition that is not usually duplicated, and one which distinctly limits the general application of these conclusions in the lower economic levels of life. Without reliable refrigeration the hazards of artificial feeding, particularly from diarrheal diseases, are much greater and the effects on growth less satisfactory than those described. The authors believe that their study gives fairly convincing support to the belief that in the average case breast milk is the best food for infants during the first three months of life, provided the supply is abundant and the progress is satisfactory. In many cases, although not in the majority, it continues to be the ideal food for a few months more. In the exceptional case it may prove to be superior to good artificial food for nine or ten months. Up to nine or ten months there is no reason for arbitrarily weaning a baby who is making good progress on the breast. It was found that most mothers were willing and desirous of continuing to nurse their babies as long as the supply was fairly good and their health was not seriously impaired, even somewhat beyond the time that the baby was gaining satisfactorily. When suitable conditions for good bottle feeding are present, and when the maternal supply is inadequate, and when the baby is failing to show good progress, there need not be the slightest hesitancy after the third month in advising weaning. When the baby cannot get at least half of its supply from the maternal breast, he should be weaned at once and spared, with its mother, the annoyances and uncertainties of mixed feeding. They found that during the first quarter of the first year breast-fed babies showed a significantly better mean rate of gain than properly bottle-

fed babies. After the first quarter of the first year, artificially fed babies showed a significantly greater mean rate of gain, and this superiority became progressively greater up to the time of weaning. In the material studied the number of infections per baby and the proportion of babies having infections were greater in the breast-fed group of the first, third and fourth quarters, and greater in the bottle-fed group during the second quarter. The number of infections in the breast-fed after weaning during the fourth quarter was greatly in excess of that in the bottle fed. There was no evidence in this series of increased resistance to infection from breast feeding, but rather evidence of greater susceptibility or greater exposure or both.

Treatment of Athreptic Nurslings by Thyroid Extract in Subcutaneous Injection.—NOBECOURT, LIEGE and GUERIN (*Arch. de méd. des Enf.*, 19**33**, 647) treated 5 cases of athrepsia by daily injections of thyroid extract subcutaneously. The usual dose was from 0.05 to 0.1 gm. of a liquid extract. Some patients did not stand the extract as well as others so that the initial dose usually was one-fourth of an ampule of a solution containing 0.1 gm. to each 1 cc. if digestive or cardiac disturbances or fever resulted, the treatment was discontinued. Although in some cases of confirmed cachexia or hypotrophy the results of the thyroid extract treatment were negligible, it was found in general to be efficacious. The first effect is usually the return of appetite. The digestive troubles are improved, the temperature curve becomes stabilized and the weight of the child increases. The time required varies with the severity and duration of the athreptic condition. Although other methods are of value in combating athrepsia in nurslings, thyroid extract has been particularly helpful in certain cases of extreme cachexia in which other methods have failed.

The Gastric and Duodenal Contents of Normal Infants and Children.—KLUMPP and NEALE (*Am. J. Dis. Child.*, 1930, **40**, 1215) studied the duodenal enzyme activity and reaction of the gastric and duodenal contents of 74 children. In determining the enzyme activity the method of McClure, Wetmore and Reynolds was used. The hydrogen-ion content was established colorimetrically by dialysis as described by Marriott and Davidson. The amyolytic enzyme was found to be feeble in children under one year of age. Beyond the first year it was excessive and exceeded the average range for adults. Following the test meal of from 30 to 60 cc. of 40 per cent cream, there was, with exceptions, an increase in amylolytic activity. The amount of lipolytic activity showed a consistently low trend throughout childhood. The values in children under one year of age were extremely low. The lipolytic activity after the test meal was uniformly greater than before. In contrast to amylolytic and lipolytic activity, the proteolytic enzyme activity was strong throughout infancy and childhood. There was no consistent variation in proteolytic activity in response to the test meal. The hydrogen-ion concentration of the gastric contents gradually declined from an average of slightly above 4 in the youngest group to 2.8 in the oldest. There was a slight tendency toward increased acidity following the test meal. The hydrogen-ion concentration of the gastric contents was thus found to be well above the optimum

range of pepsin activity. Eleven of 18 infants, or 61 per cent, showed no free hydrochloric acid during fasting and 8 of 18, or 44 per cent, showed none after the cream meal. Of the entire series 21 of 40, or 52 per cent, gave no free hydrochloric acid during fasting, and 11 of 45, or 24 per cent, produced none after the test meal. These observations emphasize the fact that unless the histamin test is used, the presence of true achlorhydria is uncertain. The hydrogen-ion content of the duodenal secretion in the fasting state showed a striking tendency at all ages to remain fixed in the vicinity of 7. Following the cream meal, the hydrogen-ion concentration fell in a constant manner to an average of slightly above 5.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

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Granular Transformation of Spirochæta Pallida in Aortic Focal Lesions.—WARTHIN and OLSEN (*Am. J. Syph.*, 1930, **14**, 433) extend a previous observation on granular degeneration of the Spirochæta pallida in the renal tubules, to similar findings in the focal syphilitic necroses of the aortic wall. The article consists of numerous excellent reproductions of microphotographs of the various stages of the degenerative process. The authors are not yet prepared to state that a submicroscopic form follows the minute granule in the series of changes which they present, nor are they willing as yet to regard as anything but guesswork the suggestion that these granular forms are phases in a life cycle of the Spirochæta pallida which has significance for the transmission of the disease.

A Study, Based on Personal Follow-up Results in a Syphilis Clinic, of the Patients' Reasons for Lapse in Treatment.—PUGH, STOKES, BROWN and CARNELL (*Am. J. Syph.*, 1930, **14**, 438) find the results of the ordinary correspondence follow-up maintained with patients under treatment in the syphilis clinic were approximately 30 per cent returns. Those obtained by personal follow-up of the type described were 64 per cent or more than double the effectiveness. The cost of personal follow-up (in this research approximately $1.40 per visit) is, however, prohibitive without special endowment for the purpose. The authors find that financial difficulties, unsuitability of hours, shortcomings of the clinic's personnel in establishing rapport and educating its patients, and painful or incommoding reactions to treatment are,

in varying proportions, depending on the method of analysis, the overwhelmingly prevalent causes for the failure of patients with syphilis to continue under treatment and supervision until discharged. Between 50 and 60 per cent of patients lost through these faults in management can be recovered by personal follow-up, and 85 per cent of the reasons for lapse included in the entire survey are capable of some degree of preventive adjustment. The authors believe that a limited experience with compulsion methods does not demonstrate their effectiveness, and that emphasis should be placed on the need for study and improvement of the clinic, its methods and operation in serving its clientèle, rather than on a mere resort to externally applied legislation and force.

Local Recurrences After Excision of the Chancre in the Rabbit and Their Immunologic Significance.—BRANDT (*Arch. f. Dermat. u. Syph.*, 1930, **162**, 157) think that, in contrast with man, recurrences of the chancre at or near the site of an excised primary lesion in the rabbit are very frequent. The trauma of the excision is not a factor in producing these recurrences. The protective effect of the chancre is borne out by these experiments, and it appears that the protection is derived from something which the chancre contributes to the general mechanism of the body, rather than to the mere local condition of the tissues. When the chancre is removed the general protective effect is, of course, removed with it, and it is notable that in those animals in which, after removal of the primary lesion, no recurrences of the chancre developed, the general immunity reaction or protection fails likewise and numerous generalized recurrent lesions ensue. It appears that the effect of excising the chancre is not, as has been supposed at times, due to the extirpation of the testis together with the primary lesion, for it appears that the presence of testicular tissue tends to bring on relapse rather than prevent it.

GYNECOLOGY AND OBSTETRICS

UNDER THE CHARGE OF

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Preradium Treatment of Cervical Cancer.—A contribution of interest to the gynecologic radiotherapist is presented by SWANBERG (*Radiology*, 1930, **15**, 290), in which he indicates some of the refinements which should accompany radium irradiation of cancer of the cervix. He believes that every case of advanced cancer of the cervix should receive external irradiation, and if this is given by high-voltage Roentgen rays it should preferably precede the internal radium treatment. Local

infection constantly accompanies cervical cancer and no case should receive radium treatment, he states, until the infection has been controlled by suitable douches. After a week or ten days of preliminary treatment the cervical canal should be gently dilated by the use of graduated uterine sounds and the length of the uterine canal noted. The patient is then returned to bed and her temperature taken at frequent intervals during a period of twenty-four hours. If there is no increase in temperature she is ready for internal radium treatment. The principal internal radium treatment should not be given until the uterine canal is patent, as the best results are secured by placing radium the entire length of the canal. If the canal is occluded it should be treated by preliminary radium treatments until rendered patent or the cervix should be amputated by electrothermic measures preceding the principal internal radium treatment. Every effort should be made to eliminate sources of focal infection and to improve the general health of the patient.

Results of Surgical Treatment of Cervical Cancer.—It is becoming more apparent every year that in order to determine the results of operation in cancer of the cervix we must scan European statistics, since the overwhelming majority of such cases in this country are treated by radium irradiation. A very excellent statistical summary in a small series of cases is that presented by BEGOUIN (*Bordeaux chir.*, April 1, 1930), who performed 75 Wertheim operations between 1904 and 1918, with 6 deaths, or 8 per cent mortality. Of the cases traced from ten to twenty-five years, 20 or 50 per cent were living and well, 5 more than twenty years, 5 more than fifteen years, 5 more than twelve years and 5 more than ten years. All of the operations were of the radical abdominal hysterectomy type with dissection of the ureters and vaginal drainage, but without ligature of the iliac vessels. In all cases general inhalation anesthesia (ether or chloroform) was used, and in many cases the cancer was well advanced, showing partial fixation of the uterus. It is not difficult to understand why the skilled continental surgeons who are able to obtain such good results are quite enthusiastic about the radical operation, but even an 8 per cent mortality as here reported, while unusually low for such a serious operation, is still considerably above the mortality attendant upon irradiation which gives about as good or perhaps better end results.

Ovarian Cysts Associated with Hydatidiform Mole.—The curious association of ovarian cystic tumors, which we term theca-lutein cysts, with hydatidiform mole and chorionepithelioma have always been of interest to the gynecologists. We know that such cysts are present in over one-half of the cases, and we also know that they usually disappear after the removal of the mole, but further than this our knowledge is limited. This subject has attracted the attention of NOVAK and KOFF (*Am. J. Obst. and Gynec.*, 1930, **20**, 481), who have had the opportunity of studying 2 cases of hydatidiform mole and 2 cases of chorionepithelioma, in all of which the ovaries were available for study, while in 1 of the cases of chorionepithelioma a histologic study of the pituitary gland was also possible. As a result of their histologic studies they believe that the anterior pituitary is the immediate cause

of the lutein hyperreaction seen in the ovaries of such cases, and that the hyperluteinization involves both the granulosa and the theca interna. The histologic study of the anterior pituitary in 1 of their cases of chorionepithelioma showed an abnormally marked and persisting pregnancy reaction. This observation, for the first time, offers a histologic explanation for the persistence of the pregnancy test long after the removal of the primary tumor, as has been reported several times. They believe this phenomenon is due to the presence of considerable masses of trophoblastic tissue in the metastases, as was the case in their patient. In short, the evidence indicates that the interreaction is a triangular one, the trophoblastic increase being responsible for the pituitary reaction, and the latter calling forth the abnormal ovarian response. The importance of such observations at the present time is especially great, because of recent developments in our knowledge of the physiologic interrelationships between the ovaries and the anterior pituitary.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Tuberculosis of the Eye.—Descriptions of typical cases of tuberculosis of the eye can be found in literature as early as 1711, but the first studies of the disease were made in the nineteenth century. As the diagnosis had to be made without the use of the ophthalmoscope, lesions originating within the globe grew to great size before they could be recognized by the appearance of a gray mass through the pupil, and often were confused with medullary sarcoma. The tuberculous character of the lesions of the choroid was demonstrated by Virchow, Cohnheim, Gerlach, Manz and others, and the similarity of these lesions to the tuberculous lesion elsewhere in the body was pointed out.

The Outstanding Features of Eye Tuberculosis.—Lloyd (*Am. J. Ophth.*, 1930, **13**, 753) are its limitations to the part of the eye involved, the tolerance of the eye to a severe local process without serious pain or redness, its insidiousness of onset in some cases and its sharpness of onset in others, its chronicity and tendency to relapse. That many of the diseases of the eye attributed to focal infection are due to tuberculosis is the conviction of the author who nevertheless believes that diseased tonsils and adenoids, infected teeth, and diseased gall bladders, Fallopian tubes and seminal vesicles should be regarded as factors in the secondary infection of a tuberculous area. It is a misconception of the character of tuberculosis to regard usual lung tuberculosis as characteristic of the single disease. Eye tuberculosis occurs as miliary tubercles or embolic processes metastatic from some other part of the body, the lungs or bronchial lymph glands. Almost all the fundus

lesions of tuberculous origin are located in the choroid, but there are cases which seem to be limited to a retinal vessel. This would suggest embolism or thrombosis, but proof would be difficult. Phlebitis and retinal hemorrhages may be due to rupture of a diseased vessel wall and primary retinal disease as opposed to the usual location in the choroid is reported. Changes in the vitreous, iris and lens eventually result from chronic lesions situated in the fundus. They may be detected early by examination of the eye with the slit lamp. In chronic cases the vision of the eye may be lost through destruction of the choroid, retina and nerve. Uveitis is a common finding in tuberculosis of the eye and is recognized as indicating a progressive, active form of the disease. For this form the author used Roentgen rays, shielded by aluminum or silver screens to exclude the rays that burn. He gives three or or four treatments with a 30 to 40 per cent skin-erythema dose. The first effect is upon the vitreous exudates which begin to clear after a single dose. Disseminated choroiditis, a common tuberculous affection simulates the lesion of syphilis and cannot be differentiated in all cases by ophthalmoscopic examination. The history and physical examination of the patient usually gives the clue to the etiology. Phlyctenules belong to the group of external eye disease of tuberculosis, though the bacillus is not found in the tissue. It is looked upon as a precursor of meningitis or pulmonary disease. While many physicians prefer to treat this condition with tuberculin the author mentions the use of quinin in some form as an efficacious remedy. Sclerosing keratitis is an extremely rare type of tuberculous disease, and some forms of arthritis deformans have eye lesions that suggest the tuberculous origin of the joint disturbances.

OTO-RHINO-LARYNGOLOGY

UNDER THE CHARGE OF

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Experimental Production of Cervical Cellulitis Resembling Ludwig's Angina.—Although almost a century has elapsed since von Ludwig described as a gangrenous induration of the neck the condition which now bears his name—angina ludovici—the mortality still is estimated at from 40 to 50 per cent. Fortunately the disease is not common; neither is it rare. Evidently beginning around the lower teeth, the infection involves the floor of the mouth and extends into the deep fascial planes of the neck, producing an intense cellulitis. The pyogenic cocci—especially streptococci—have been incriminated in the majority of cases, but lately the fusospirillary organisms of Vincent have been found in the cervical exudate. With this in mind, SMITH (*Proc. Soc. Exper. Biol. and Med.*, 1930, **27**, 941) injected scrapings from the gingival margins of patients with pyorrhea alveolaris into the inner

margin of the gums in 5 guinea pigs. One developed a cellulitis of the neck. A passage experiment of the fuso-spirochetal-laden exudate in 10 pigs produced an unilateral brawny cervical induration in 7,—5 of which died. Nine out of 10 additional animals similarly injected developed a cervical cellulitis resembling Ludwig's angina. Cultures from all of these 17 pigs yielded spirochetes, fusiform bacilli, vibrios and anaërobic cocci. To date, the only weapon at our disposal has been early recognition and extensive incisions. Inasmuch as neoarsphenamin or sulpharsphenamin have been beneficial in combating fuso-spirochetal infections of the lung, Smith quite properly suggests arsenical therapy in those cases of Ludwig's angina due to these anaërobic bacteria.

Etiology of Asthma: Relation of Sinus Infection to Asthmatic Attacks.—Convinced that etiologically there must be two classes of asthma—one due to allergy and the other due to toxicosis and nasal infection, POTTS (*Arch. Otolaryngol.*, 1930, **12**, 72) quotes McGinnis: The medical man who believes the causative factor to be protein absorption . . . , the surgeon who believes only in nasal surgery, and the physician who believes only in the theory of deficient calcium content in the blood could benefit by a consideration of all the possibilities. It is evident that it takes more than simple nasal irritation and infection to cause asthma, the added factor being "probably toxemia secondary to infection." Experience prompts the author to conclude that those cases of well-established asthma, with severe chronic sinusitis and usually with polyposis, require for relief the same thorough eradication of the diseased tissues "as has been so ably advocated by the leaders of the medical profession for diseases due to focal infections."

The Prognosis of Operations for Removal of Nasal Polypi in Cases of Asthma.—Polyposis nasi is associated not infrequently with bronchial asthma; and much clinical evidence is at hand to indicate an etiologic relationship between these two conditions, both of which, however, are essentially symptomatic—whether subjectively or objectively—rather than clinical entities *per se*. Just as morphology is not always a reliable index to function, neither can there be a certainty that removal of a given morbid process will effect a desired result either local or systemic. In other words: "experimentum periculosum; judicium difficile." This is especially true in attempting to forecast the ultimate influence of operative removal of nasal polypi on the course of asthma. The problem is important and any information aimed at its clarification is welcome. To this end, FRANCIS (*Practitioner*, 1929, **123**, 272) has found in a study of 24 cases that: if a patient can take acetylsalicylic acid, the removal of nasal polypi will be likely to benefit the asthma, whereas in those intolerant of this drug the asthma often is worse following intranasal surgery—particularly in those individuals with a low systolic blood pressure. The author cautions against the administration of acetylsalicylic acid to asthmatics with polyposis nasi and hypopiesis or to patients with nasal polypi without asthma but with a low blood pressure.

ABSTRACTOR'S NOTE.—Intranasal tamponade of colloidal silver is of diagnostic, therapeutic and prognostic value in many of these cases.

RADIOLOGY

UNDER THE CHARGE OF

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Roentgenologic Signs of Gastrojejunal and Jejunal Ulcer.—The direct roentgenologic signs which, according to CAMP (*Radiology*, 1930, **15**, 274) permit a positive diagnosis of gastrojejunal or jejunal ulceration are: (1) The presence of an ulcer niche; (2) persistent deformity of the stomach, stoma or jejunum; (3) the presence of gastrojejunocolic fistula; (4) closure of the stoma. It is the author's impression that a niche may be seen in about 60% of the cases. Most niches are found in the jejunum, nearly always in the efferent loop, and sometimes as far as 15 cm. from the stoma. The usual shadow of the niche is slightly less than 1 cm. in diameter and projects from the lateral border of the efferent loop, frequently close to the stomach. It frequently resembles in appearance one of the budlike diverticula often found in the colon. Deformity of the stomach, stoma or jejunum produced by the associated inflammatory reaction is the most common change accompanying gastrojejunal or jejunal ulcer. The deformity of the stomach usually seen with ulceration at the stoma appears as a puckering of the gastric contour about the opening, with deformity of the rugæ. In many cases in which the stomach empties rapidly the stoma and contiguous portion of the jejunum have a tubular or funnel-like appearance, indicating inflammatory induration. Deformity of the jejunum is manifested as persistent narrowing, with retraction or irregularity of the outline, and may be localized or diffuse. It occurs most commonly in cases of jejunal ulcer, but may also be associated in a lesser degree with ulceration at the stoma. Within the deformed area the valvulæ conniventes are obliterated, and this distinguishes it from deformity due to adhesions. In the absence of a malignant lesion the presence of gastrojejunocolic fistula is evidence of preceding jejunal or gastrojejunal ulceration, whether or not other signs are present. Verbrugge, in a review of the cases of gastrojejunal ulcer at the Mayo Clinic, found that gastrojejunocolic fistula has developed in 11%. The barium meal alone should not be relied on to show a fistula, for frequently it can be discerned only by means of the opaque enema.

Amniography.—A method is described by MENEES, MILLER and HOLLY (*Am. J. Roent. and Rad. Therap.*, 1930, **24**, 363) for visualizing the fetal soft parts, localizing the placenta and occasionally determining the sex of a fetus. It may be of value in the diagnosis of placenta previa and determining the exact relation of the placenta to the cervical canal. To obtain contrast, a 1 to 1 solution of U. S. P. strontium iodid

is injected through the interior abdominal wall into the amniotic cavity. After anesthesizing the skin with novocain, a small flexible lumbar puncture needle is passed into the amniotic cavity, usually below the umbilicus. After obtaining fluid through the needle injection is made slowly with frequent withdrawals of amniotic fluid to dilute the solution. Films are made after one-half to one hour, the patient changing position frequently to assist in mixing. From 9 to 10 cc. of the solution will be sufficient for the average case in the later months of pregnancy. In 21 cases of normal pregnancy there were no ill effects to mother or fetus. In a case of placenta previa at the sixth month the fetus was expelled about thirty hours after injection. The location of the placenta was shown in the majority of cases. The cord encircling the fetal neck was shown twice. Sex was determined 4 times: 3 males and 1 female.

NEUROLOGY AND PSYCHIATRY

UNDER THE CHARGE OF

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The Brain-liver Weight Ratio in Insanity.—FLEMING (*J. Ment. Sci.*, 1930, **76**, 265) compares his findings on the brain and liver weights of 157 epileptics in a series of 1932 autopsies with those found by previous observers and those found in other forms of mental disease. He considers that his results show definitely that in neither emaciated nor nonemaciated epileptics of either under or over fifty years, does the degree of atrophy of the liver and brain differ from that of the group of psychoses in general and the brain-liver weight ratio deviates less from the normal than in other psychoses. In the psychoses in general in the nonemaciated of less than fifty years of age there is a well-marked decrease in weight of both the liver and the brain. The decrease in the two organs runs parallel, so that the brain-liver weight ratio in this group remains at the normal, 0.87.

A Note on Some Postmortem Blood Changes Observed in Epilepsy.—PATTERSON, WEINGROW and PATTERSON (*Psychiat Quart.*, 1930, **4**, 367) reports a study of blood changes observed in tests made on material obtained from 13 autopsies. Briefly, they found that coagulation time was markedly postmortem; blood platelets were seldom seen in the films prepared after circulation had ceased; the erythrocytes showed anisocytosis, poikilocytosis and altered chronic reactions; the leukocytes showed varying stages of disintegration; eosinophils and endotheliocytes could not be recognized in the smears; crystals were sometimes seen in the films; preparations from internal viscera exhibited no other significant changes except the introduction of cellular forms not belonging properly to blood as a tissue; red, white and differential

counts could not be performed satisfactorily after death because of difficulty caused by the altered conditions. They contend that these results can all be explained on the change of the blood plasma from an isotonic to a hypertonic medium after death.

The Problem of the Anatomy of Schizophrenia.—SPIELMEYER (*J. Nerv. and Ment. Dis.*, 1930, **72**, 241) discussess the probability of an organic basis for dementia præcox and concludes, in view of the fact that he believes changes to be clearly demonstrable (in the nature of a cellular loss in the third layer of the cortex as well as in the deep layers, with, sometimes, an enormous fat accumulation) that dementia præcox is an organic process. He argues that, although many cases of dementia præcox show normal brains at autopsy, nevertheless, negative findings can never be accepted as conclusive evidence. He does not consider that the findings point to any specific process but considers them to be indicative only of any organic basis for dementia præcox. "These findings only indicate the organic nature of schizophrenia, not, however, the anatomic diagnosis and the differential diagnosis which we need so very much."

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Hydatid Cyst. A Review and Report of Cases from North China.—Hydatid disease is reported from many countries, and although its transmission is in relation to the infestation in dogs, these animals alone do not determine the varying incidence in any one district. In not a few countries the incidence of the human infection is in direct relation to the infestation of sheep, which act as hosts for the same phase of the life cycle of the parasite as does man. The opportunity for the retransference from dog to sheep and the reverse, maintains a fairly high endemic character. LOUCKS (*National Med. J. of China*, 1930, **16**, 402) reports upon the not uncommon presence of hydatid disease among the inhabitants of Northern China. These people are interested in sheep raising, which industry has been growing in recent years. In a period of a little over ten years the author has collected 16 cases, appearing at the Hospital of the Union Medical College, Peiping. Eleven of these cases came to operation. In 6 cases the liver alone was involved, in 2 the liver and peritoneum, in 1 the liver and spleen, in another the liver, spleen, bone and muscle, while in a single case the cyst was located in the orbit alone. The diagnoses were made by the demonstration of the characteristic cyst with its contents. The author discusses the various accessory methods for the diagnosis of this disease,

though he has had no direct experience with the complement-fixation test, precipitation test, or the intradermal test. In the early stages of the cyst development the diagnosis is very difficult, based on clinical methods alone. The knowledge of the patient's habits and the region in which he lives is often suggestive in the presence of other signs of the hydatid disease.

The Rous Sarcoma No. 1: Loss of Filtrate Activity at Incubator Temperature: Protection by Means of Hydrocyanic Acid.—Active filtrates of the Rous Sarcoma No. 1 have been shown by GYE and PURDY (*Brit. J. Exper. Path.*, 1930, **11**, 282) to develop a perceptible clouding with precipitate within four hours of the commencement of incubation at 37° C. The amount of precipitate formed depends upon the concentration of protein in the filtrate. Coincidental with the formation of the precipitate there is a steady loss of power of the extract to produce tumors when injected into normal fowls. However, the earliest appearance of turbidity precedes the earliest detectable loss of potency, and precipitation continues after the filtrate has become completely inactive. The authors found that hydrocyanic acid in dilutions as low as 1 in 50,000 protected the filtrate against loss of activity during incubation for a period of forty-eight hours and even longer. Cyanid also prevented the formation of precipitate, the filtrates remaining clear for many hours after the commencement of incubation. Cystein was found to be even more effective in preventing precipitation. Filtrates protected by cystein, however, lost their potency within about three days, even though the fluid remained clear for periods up to a week.

Tar Cancer in Mice: (1) The Technique of the Comparative Experiment.—WATSON and MELLANBY (*Brit. J. Exper. Med.*, 1930, **11**, 267) have described a method of experimental procedure whereby groups of mice, all treated with tar, may be compared with a view to determining the effects of slight variations of conditions among the various groups of animals. One group in each experiment is maintained on the control diet and invariably treated in the same way regardless of which experiment it forms a part. The other groups were subjected to different conditions of diet, care being taken to vary only one factor at a time. The variation consisted of substitution of an aliquot portion of the diet in each group by a different foodstuff of animal origin. In an experiment lasting 480 days no definite differences were found in the reaction of the mice on the different diets to the treatment with tar. One feature of interest was that the tumor bearing animals had practically twice the life span of the other mice and indeed, usually lived longer in spite of the skin tumors than did the mice which were alive at the end of the tar treatment and which never subsequently developed skin tumors Of 255 mice with skin tumors, 52.4 per cent showed typical tumor nodules of lung after fixation for forty-eight hours in formol saline. In normal untarred mice of the same breed such nodules were found in only 6 per cent after similar fixation of the lungs.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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An Outbreak of Food Poisoning Proved to be Due to a Yellow Hemolytic Staphylococcus.—DACK, CARY, WOOLPERT and WIGGERS (*J. Prev. Med.*, 1930, **4**, 167) report 11 cases of food poisoning due to two sponge cakes. The illness was typical acute gastroenteritis with nausea, vomiting, diarrhea and marked prostration in the acute cases and nausea, epigastric distress and diarrhea in the cases with delayed symptoms. No deaths occurred. All components of the cake (icing, cake substance, and so forth) were innocuous when fed to monkeys, rabbits and mice, but when fed to human volunteers, the cake substance proved to contain a toxic factor. Three types of organisms predominated in the layer portion of the cake. When veal-infusion-broth filtrates from these strains were injected intravenously into rabbits, the only one that proved toxic was that from a yellow hemolytic staphylococcus. Human volunteers who drank different amounts of this same filtrate developed definite symptoms of food poisoning similar to those of the individuals eating the original cake. Intravenous injections of rabbits with veal-infusion-broth filtrates of the toxic staphylococcus (twenty-four-, forty-, forty-eight-hour cultures) resulted in either profuse watery diarrhea and death, or no diarrhea and death, autopsy in the latter case revealing fluid and gas in the abnormally distended cecum, and stasis in the colon. These changes present an interesting correlation with the results observed in the persons receiving 10 cc. and 5 cc. amounts of the filtrate. Similarly prepared filtrates of known *Staphylococcus aureus* and *Staphylococcus albus* cultures, when injected intravenously into rabbits, yielded negative results. A few heat-lability experiments showed that the viability of the organism was destroyed by exposure to 80° C. for fifteen minutes. The potency of the toxic factor was slightly attenuated, but certainly not eliminated, in filtrate subjected to 100° C. for thirty minutes, as tested by subsequent intravenous injections of rabbits.

Loss of Actinic Intensity in Urban Sunshine Due to Air Pollution.—TONNEY, HOEFT and SOMERS (*J. Prev. Med.*, 1930, **2**, 139) made observations of the loss of solar ultraviolet light values in Chicago, due to atmospheric pollution, over a period of about three years. Simultaneous hourly readings on days selected for uniform weather conditions were made at clear points outside the city and at designated stations within the city, including the loop and three other sections. Material loss of the ultraviolet intensity available at the clear points was demonstrated

in all the urban districts tested, at all seasons of the year. The percentage loss was greatest in the warm months when the concentration of the shorter ultraviolet waves is greatest. The least percentage loss and the lowest absolute intensities were observed in the cold months, when only the longer rays of the ultraviolet spectral region are present in significant amounts. The lake shore districts of the city showed relatively less loss of ultraviolet light than the stations farther inland. The high percentage loss of short ultraviolet waves in summer, the season of minimum smoke production, suggests that the improvement to be expected from smoke-abatement methods applicable to existing combustion processes will not in reality solve the problem, and seems to justify the view that the general substitution of electric energy for combustion processes as a source of heat, light and power is the logical ultimate solution.

PHYSIOLOGY

PROCEEDINGS OF

THE PHYSIOLOGICAL SOCIETY OF PHILADELPHIA

SESSION OF JANUARY 19, 1931.

Observations on Pigment Migration Within the Fish Melanophore.—SAMUEL A. MATTHEWS (from the Department of Anatomy, University of Pennsylvania). When the scales of Fundulus are mounted in tissue culture preparations their melanophore processes become so readily visible that they can be studied even when free from pigment, the cells themselves remaining active for several days. Careful measurements failed to detect any change in the diameters of these processes during either central or peripheral migration of the pigment granules. The fish melanophore is in no sense amœboid.

The pigment in a melanophore process isolated from its cell by means of a microneedle can still spread itself over a wide field or concentrate in a small area, even when the body of the cell has been destroyed. Hence the centrosphere exerts no essential influence on pigment migration within melanophore processes.

The differences in physical condition of a melanophore with expanded pigment as contrasted with one with contracted pigment tend to support Spaeth's interpretation of the mechanism of melanophore "contraction," that is, that this "contraction" is possibly a reversible coagulation process such as commonly occurs in emulsoids.

Newly Described Types of Cells in the Cerebellum.—W. H. F. ADDISON (from the Department of Anatomy, University of Pennsylvania). The pattern of the cerebellar cortex is so uniform that any departure from it attracts attention. There have been described in recent years three varieties of cells which are additional, in some respects, to those shown in the usual schema. They are the synarmotic

cell of Landau; the large aberrant cells seen in the porpoise, elephant and whale; and the special associative Purkinje cells of Lorente de Nó.

The synarmotic cells were described by LANDAU (*Anat. Anz.*, 1927, **62**; *Zeits. ges. Neur. u. Psych.*, 1929, **122**) and studied by his associates BUBENAITÉ (*Medicina, Lithuania*, 1929, **10**) and KESIUNAITÉ (*Bull. Hist. appl. á la Physiologie*, 1930, **7**). They were seen in Golgi preparations, as large cells, in the granular layer and in the subjacent white matter. Their processes extend across the lamella, joining the granular layers of opposite sides of the lamella. They thus differ from the usual Golgi cells, Type II, in having axones which do not arborize in the immediate vicinity of the cell body, but at some distance from it. In Fig. 57 of vol. ii of his Histologie du Système Nerveux, Cajal shows a Golgi cell with its axone ramifying on both sides of the same lamella. There are thus certain points in common between this and the synarmotic cell of Landau.

In the cerebellar cortex of the common porpoise I have noted conspicuous large cells, scattered through the granule layer and in the adjoining white substance (*Anat. Rec.*, 1930, **45**, 204). In size they were comparable to the Purkinje cells, and were often larger. Their shape was variable, but in general they were of two forms: (1) narrow, elongated, and (2) stellate, multipolar. They were constantly present, two or three to a folium. Similar large cells are found in the cerebellar cortex of Elephas and Balaenopters, as described by OBERSTEINER (*Arb. Neur. Inst., Wien. Univ.*, 1913, **20**). Thus in three large mammals there are extremely large cells in the granular layer and white matter. In these forms there are also Golgi cells of the usual size in the granular layer, so that the large cells seem to be an additional type. However, the location of the cell-bodies is comparable to that of the synarmotic cell, and there may be some relationship.

Lorente de Nó has described a special associative type of Purkinje cell, which places in relationship distant cerebellar lamellæ (*Trav. lab. recher. biol. Mardrid*, 1924, **22**). The axone of this form of Purkinje cell transverses the medullary layer to reach the central white substance. Here it divides into several fibers, which run to distant parts and end as climbing fibers along the body and dendrites of the Purkinje cells. The beginning and ending are within the cerebellar cortex, hence the term associative. The anatomic observations on which this is based are not given in detail.

Whether these several cells are to be regarded as new cell types or merely as special forms of the usual types is still a subject for study, and is to some extent dependent upon the exact definition of the classical cell types.

The Influence of the Base-binding Power of Hemoglobin Upon Osmotic Hemolysis.—M. H. JACOBS and A. K. PARPART (from the Laboratory of Physiology, University of Pennsylvania). By means of the method previously described by one of the authors it is possible to compare accurately the osmotic effects on erythrocytes of solutions whose osmotic pressures differ by only a few tenths of 1 per cent. In working with a method of such delicacy careful control of the factors, pH, temperature and to a lesser extent oxygen tension have been found to be necessary. In the present investigation an attempt has been made

to evaluate and to explain the nature of the effects produced by these factors. It has been found that within the range studied a change in pH of 0.5 units is roughly equivalent to a change in concentration of 0.01 M NaCl and that a change of 0.01 unit should therefore produce measurable osmotic effects. With temperature, the effect of a change of 20° is equivalent approximately to a concentration change of 0.01 M NaCl, and a change of 0.5° C. has a noticeable influence on the experimental results. The effect of oxygenation is less striking, the maximum effect obtainable with ox blood being of the order of magnitude of that produced by a concentration change of 0.0016 M NaCl. In view of these facts, it is pointed out that "fragility" studies made without control of at least temperature and pH are of doubtful value. In an attempt to explain the results obtained, there has been derived by an application of the methods of van Slyke, Wu and McLean the following equation:

$$\frac{W_1}{W_2} = \frac{2R + 1 - F_1 \cdot C_2}{2R + 1 - F_2 \cdot C_1}$$

in which W is the amount of water contained in an erythrocyte, F the amount of base bound by unit amount of hemoglobin, C the concentration of the external solution and R the ratio of base to hemoglobin in the erythrocyte. By taking from the literature the best obtainable data concerning R and F, it is shown that the observed results are in good agreement with those calculated by means of the equation, and it is concluded that the factors pH, temperature, and oxygen tension, under the conditions here dealt with, influence hemolysis primarily through the osmotic effects produced by changes in the amounts of base bound by hemoglobin.

Myeloid Metaplasia in the Exteriorized Dog Spleen.—G. M. Robson and R. P. Custer (from the McManes Laboratory of Pathology, University of Pennsylvania). Myeloid metaplasia has been produced experimentally by many workers and used as a means for study of the histogenesis of blood elements. Previous observers have differed widely in their conceptions of the myelopotent cell and the mechanism of formation of the metaplastic foci. One group has held that the foci are metastatic from the bone marrow; another that they arise through differentiating mitoses of cells preëxisting in the affected tissue. A third view goes further by stating specifically that the capillary endothelium is erythropotent, while still a fourth holds that myeloid metaplasia owes its origin to cells of the circulating blood, namely, lymphocytes (hemocytoblasts).

Our observations on myeloid metaplasia are confined to cells of the erythrocyte series. Our method for induction of this phenomenon is the production of severe secondary anemia in dogs with exteriorized (Barcroft technique) spleens. Foci of red blood cell formation uniformly appear in the spleens of such animals when their circulating blood shows evidence of active blood regeneration by an increase in the reticulocyte count and the appearance of nucleated red forms. With recovery from the anemia, the metaplasia disappears, but can be reëstablished at will by the same procedures. It matters not by what method the anemia is produced, whether by hemorrhage, hemolytic

agents, or bacterial infection; observations in the spleen are uniform. Metaplasia occurred in each of the 7 animals studied and was repeatedly produced in most of them. The splenic reaction was observed by frequently repeated thin biopsies, the tissue being immediately fixed. This method of study offers the obvious advantage that the material is removed from the living animal and that the development and course of the metaplasia can be followed in the same individual.

The first change observed is a hyperplasia of the splenocytes, sinusoidal endothelium and cells of the so-called germinal centers, mitotic figures being numerous. Soon, groups of cells with richly chromatic nuclei appear in the red pulp, definitely identifiable as erythroblasts; many of these groups lie within spaces lined with hyperplastic endothelium. In richly cellular areas, groups with a similar outline are observed, but here their relation to endothelium is obscured. At this stage we have difficulty in distinguishing between hyperplastic endothelial cells and early erythroblasts; many typical cells of each type are present, but intermediate forms are numerous which apparently represent transition stages. This is particularly striking in groups of cells surrounded by a definite endothelial layer. Here one sees in the lumen typical erythroblasts; at the margin are typical hyperplastic endothelial cells; between lie cells bearing morphologic characteristics of each. The impression thus gained from study of such a cell group is the direct descent of the erythroblast from the capillary endothelium. Throughout, mitotic figures are prominent and are seen both in the endothelial and erythroblastic cells; later normoblasts are seen with greater frequency and almost invariably lie in the center of such cell groups. Blood does not circulate through these capillary sinusoids containing immature red blood cells, but we have seen that their lumina are continuous with channels containing whole blood.

We believe, therefore, that these observations support the view that, in erythrocytic myeloid metaplasia, the red blood cells are formed within endothelial-lined channels and that the capillary endothelial cell is erythropotent.

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